Southern Medical Journal

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

JUNE, 1956 Volume 49 Number 6

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Southern Medical Journal

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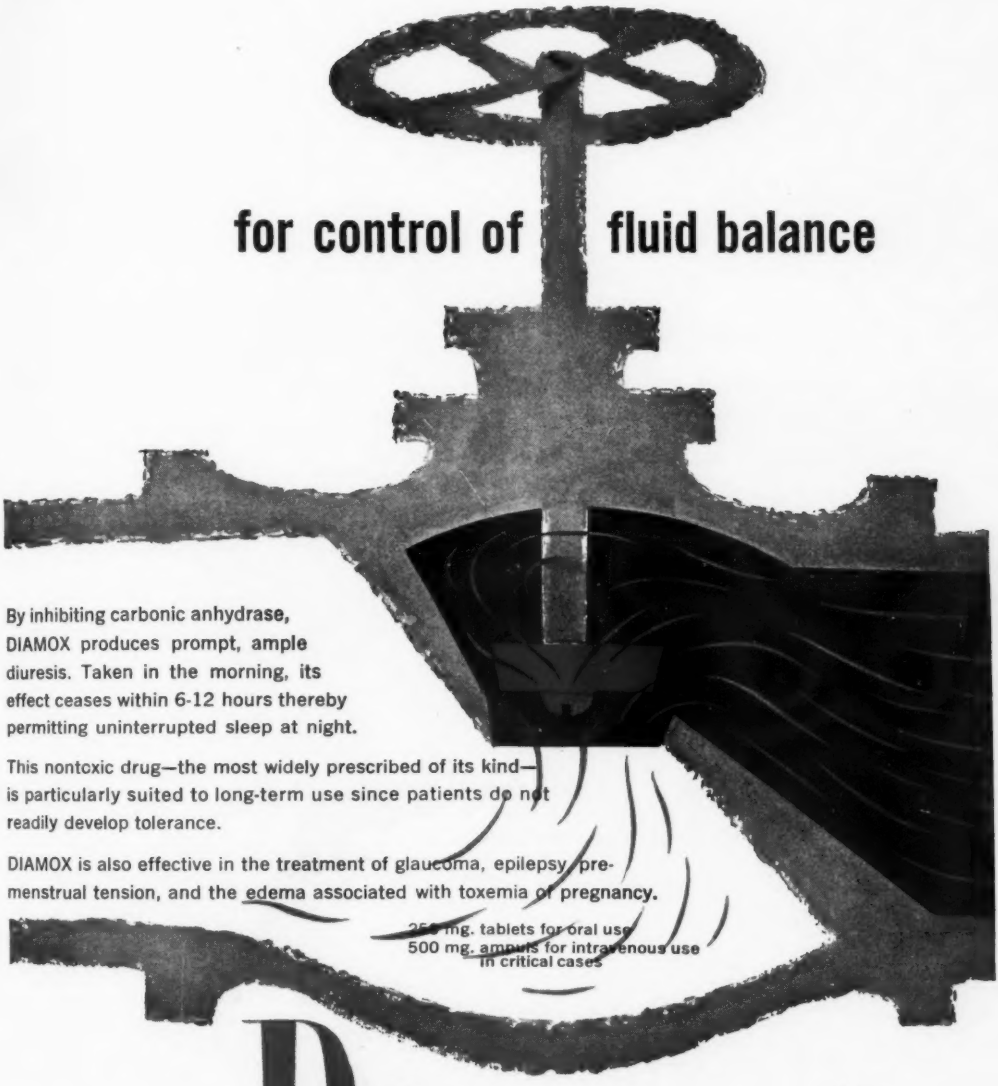

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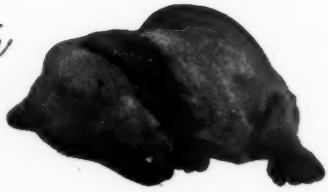

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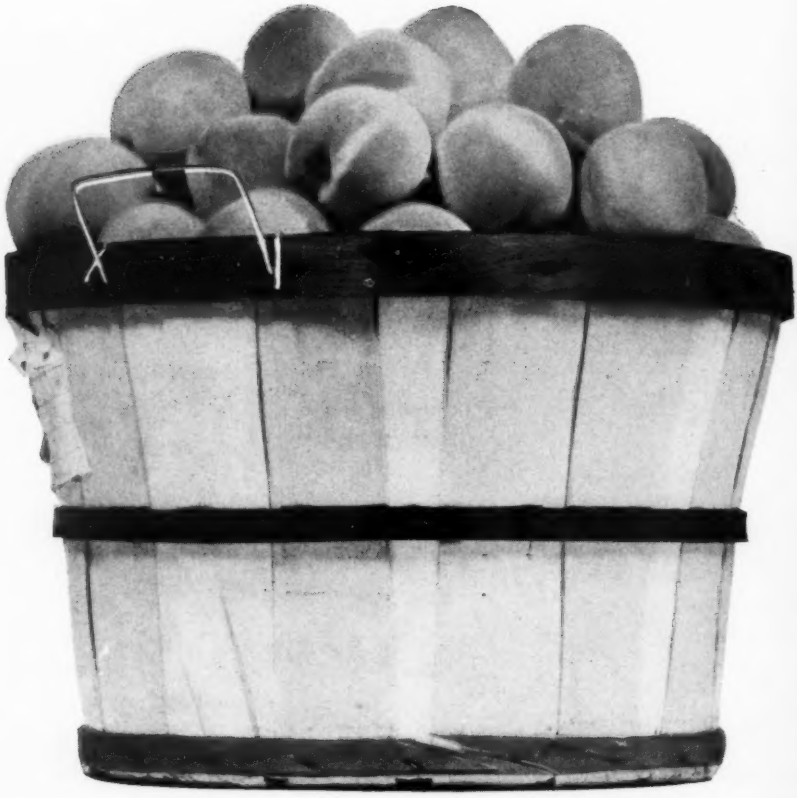

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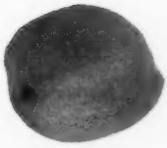

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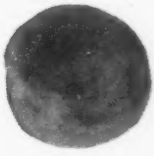

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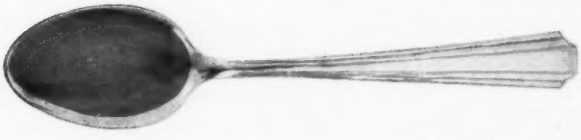

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One tablet after each meal and at bedtime. Children 1 year or over, 0.6 cc. (10 drops); infants less than 1 year, 0.3 cc. (5 drops) once daily diluted with water, milk, fruit or vegetable juice.

1. Holly, R. G.: Anemia in Pregnancy, Obstet. & Gynecol. *5*:562 (April) 1955.
2. Quilligan, J. J., Jr.: Texas State J. Med. *50:* 294 (May) 1954.
3. Hopps, H. C.; Stanley, A. J., and Shideler, A. M.: Polycythemia Induced by Cobalt, Amer. J. Clinical Path. *24:* (Dec.) 1954.

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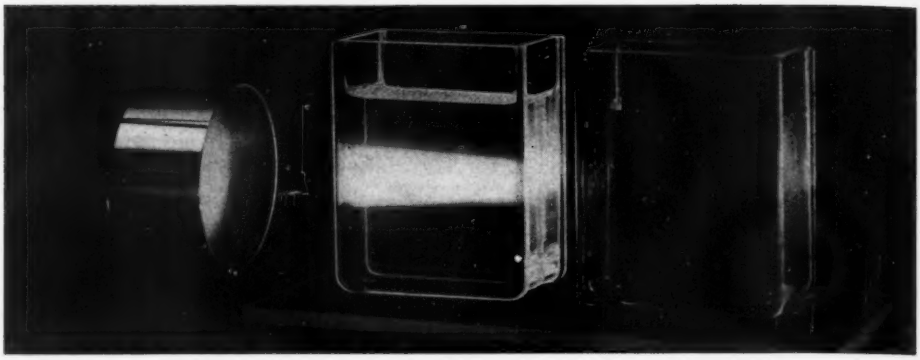

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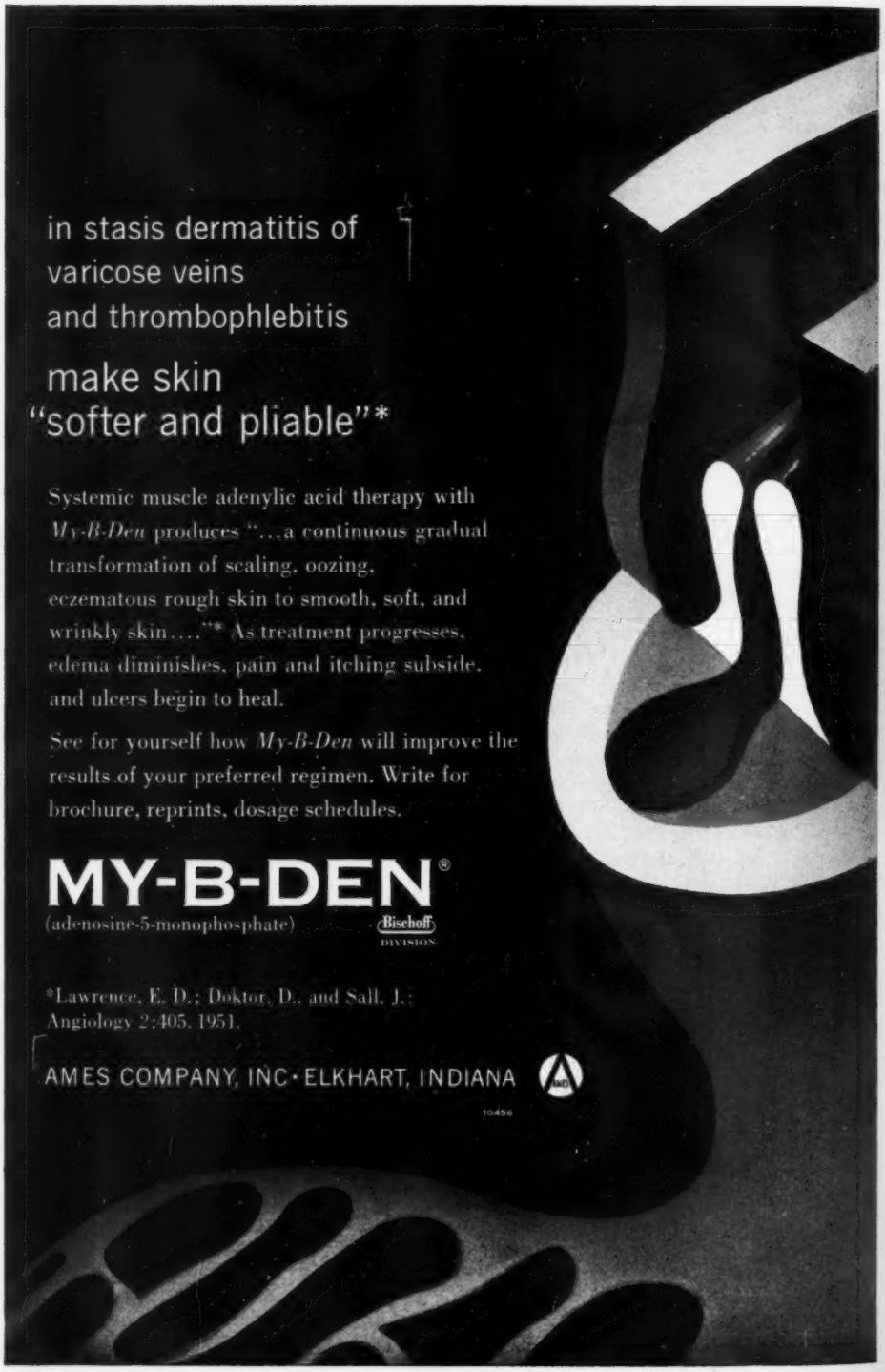
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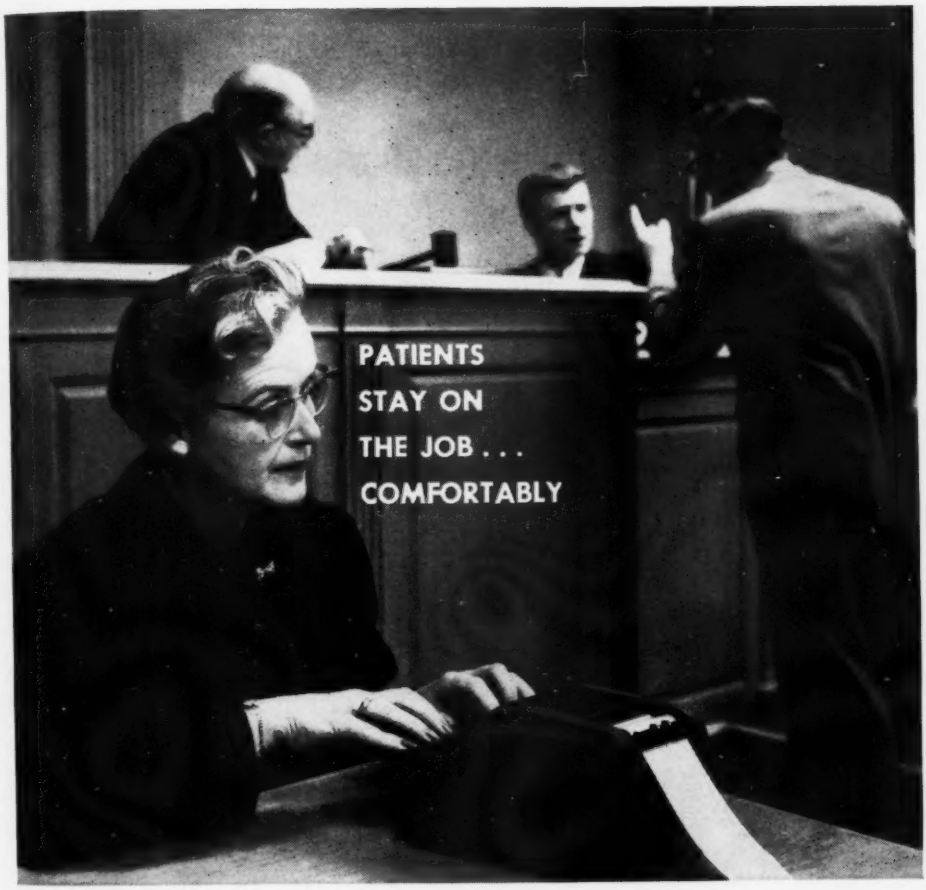

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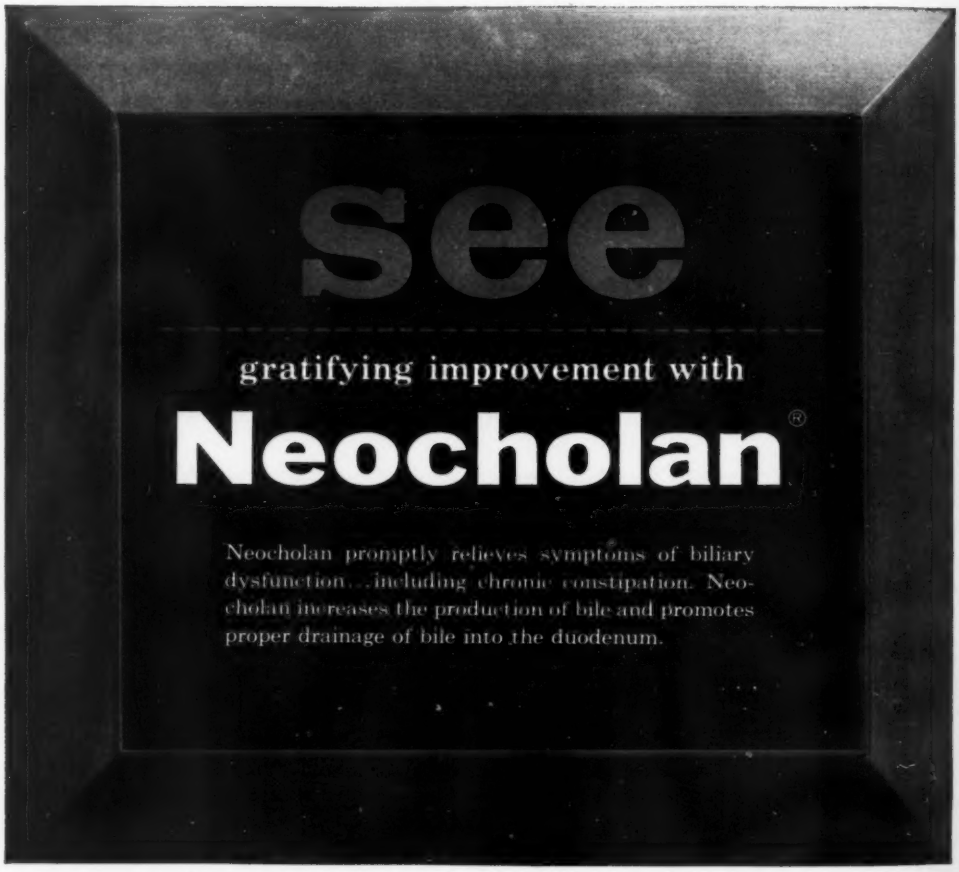
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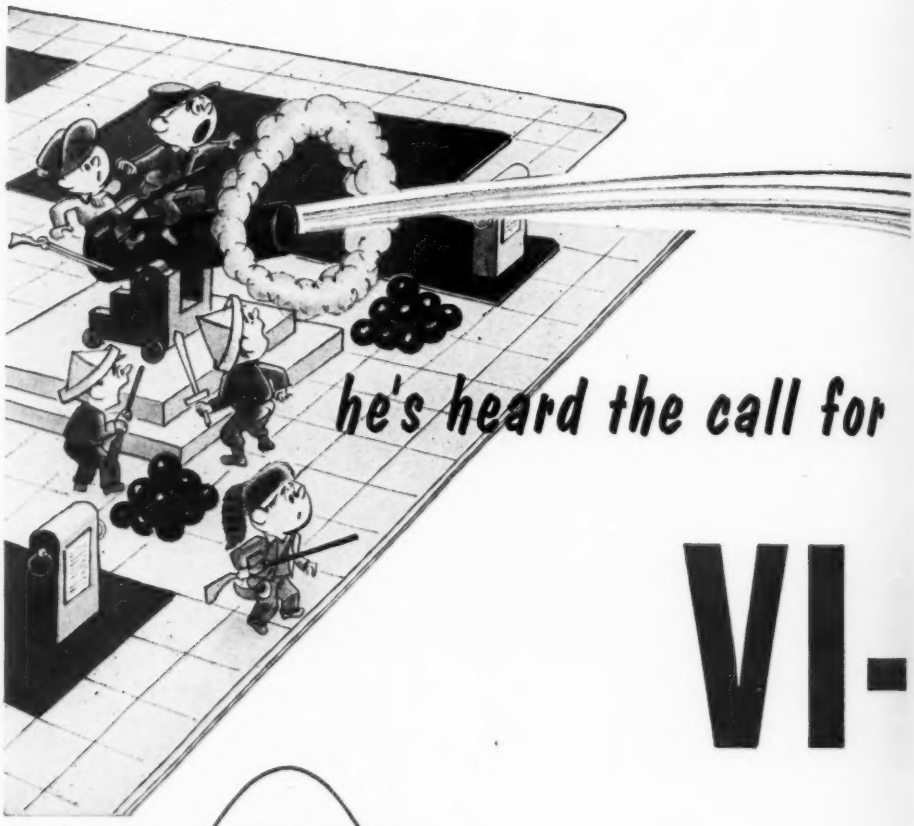

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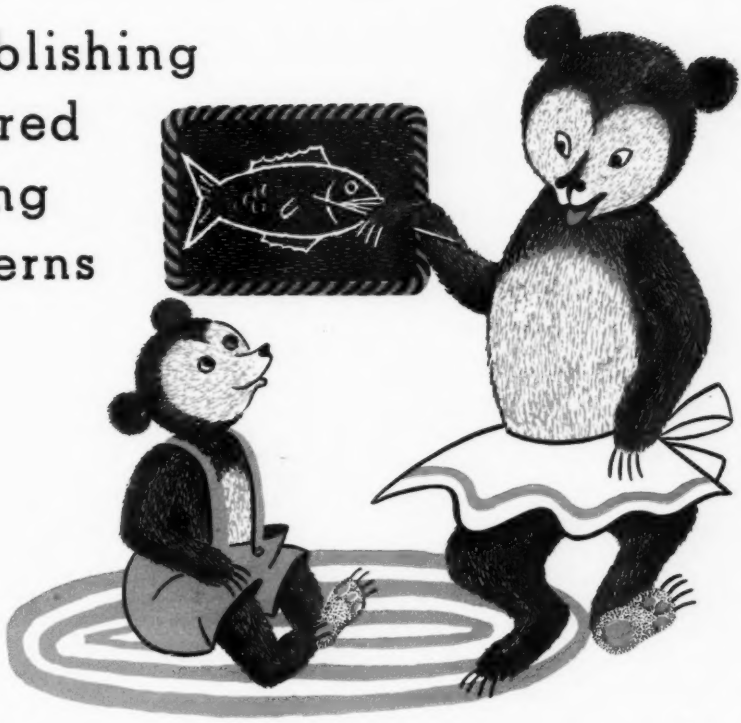
*T.M.—Cortrophin Available in other countries as Cortrophine-Z †Patent Pending

establishing desired eating patterns



Obedrin®

and the 60-10-70 Basic Plan

In the development of good eating habits, medication is important, not only in initiating control, but also in maintaining normal weight.[1,2,3]

Obedrin contains:

- Methamphetamine for its anorexigenic and mood-lifting effects.
- Pentobarbital as a balancing agent, to guard against excitation.
- Vitamins B_1 and B_2 plus niacin to supplement the diet.
- Ascorbic acid to aid in the mobilization of tissue fluids.

Since Obedrin contains no artificial bulk, the hazards of impaction are avoided. The 60-10-70 Basic Plan provides for a balanced food intake, with sufficient protein and roughage.

Formula

Semoxydrine HCl (Methamphetamine HCl) 5 mg.; Pentobarbital 20 mg.; Ascorbic acid 100 mg.; Thiamine HCl 0.5 mg.; Riboflavin 1 mg.; Niacin 5 mg.

1. Eisfelder, H.W.: Am. Pract. & Dig. Treat., 5:778 (Oct.) 1954).
2. Sebrell, W.H., Jr.: J.A.M.A., 152:42 (May, 1953).
3. Sherman, R.J.: Medical Times, 82:107 (Feb., 1954).

Write for 60-10-70 Menu pads, weight charts, and samples of Obedrin.

THE S. E. MASSENGILL COMPANY
BRISTOL, TENNESSEE

HOW OLD IS OLD?

"The really old people are those 10 years older than myself."[1]

"In the lay mind, anyone past 60 is ready for the discard . . ."[2]

". . . there are only three principal phases in the span of life: infancy, adolescence and senescence."[3]

"One finds alert, interesting, active folks in the 80's and, on the other hand, there are people in the 20's and 30's who have all the characteristics of old age."[4]

THE REAL QUESTION

To the physician on the firing line of daily practice, the question of "how old is old?" seems academic. To him, a more valid question is "How can I allay the effects of the aging process?"

FIVE PROBLEMS IN AGING

The answer, according to most authorities, is manifold, for five treatable problems seem to predominate. One, obviously, is gonadal hormone decline. Another is mild anemia. A third is the decreased production of gastric and digestive enzymes. Mineral-vitamin deficiency is the fourth. And the fifth – perhaps most important – is inadequate high-quality protein intake.

THERAPY FOR AGING

Judging from this confused clinical picture of aging, therapy for the problem would appear difficult. However, most physicians agree that a product which could correct most or all of these five commonest problems would remove past obstacles to satisfactory response. Such a product would, essentially, be true "preventive geriatrics."

NEOBON'S COMPREHENSIVE FORMULA

NEOBON®, a product of Roerig research, is a blended combination of the five most commonly indicated factors for prevention or treatment of the nonacute conditions of aging. Each soft, soluble capsule provides:

Non-stimulatory gonadal hormone replacement

balanced hematinic component

digestant enzyme replacement

specially formulated mineral-vitamin combination

new lysine, for protein improvement*

* Protein deficiency among the aging apparently stems from their excessive intake of white-flour foods which furnish incomplete protein of low biologic value. White bread protein, for example, has been shown by nutrition studies in animals[5] to be deficient only in the amino acid, lysine. In human subjects metabolic determinations indicate that the addition of supplemental lysine to a basal white-flour protein diet can convert a negative nitrogen balance into a positive one.[6]

A WORD ABOUT SYMPTOMATOLOGY

In spite of jokes to the contrary, the patient who states in the professional office that "old age is creeping up" is a rare bird indeed.

Seldom is old age the presenting complaint. Thus the physician, after correcting the specific complaints, must re-evaluate the whole person to judge his candidacy for "preventive geriatrics."

Such people have much to gain from NEOBON therapy. The rewards are fuller, more active, more pleasurable years for patients past 40. The daily dose (3 capsules) of NEOBON provides:

L-lysine	150 mg.
Methyltestosterone	3 mg.
Ethinyl Estradiol	0.018 mg.
Pancreatic Substance***	150 mg.
Glutamic Acid	90 mg.
Rutin	15 mg.
Vitamin A (Palmitate)	6,000 U.S.P. Units
Vitamin D (Irradiated Ergosterol)	600 U.S.P. Units
Vitamin E (as Tocopheryl Acetate)	15 I.U.
Calcium Pantothenate	15 mg.
Thiamine Mononitrate (Vitamin B_1)	1.5 mg.
Riboflavin (Vitamin B_2)	1.5 mg.
Pyridoxine Hydrochloride (Vitamin B_6)	1.5 mg.
Niacinamide	150 mg.
Ascorbic Acid (Vitamin C)	150 mg.
Vitamin B_{12} (Oral Concentrate)	3 mcg.
Folic Acid	0.3 mg.
Liver-Stomach Substance**	300 mg.
Iron (from Ferrous Gluconate)	10.2 mg.
Cobalt (from Cobaltous Sulfate)	0.1 mg.
Molybdenum (from Sodium Molybdate)	2 mg.
Copper (from Cupric Sulfate)	1 mg.
Manganese (from Manganous Sulfate)	1 mg.
Magnesium (from Magnesium Sulfate)	6 mg.
Iodine (from Potassium Iodide)	0.15 mg.
Potassium (from Potassium Sulfate)	5 mg.
Zinc (from Zinc Sulfate)	1.2 mg.

**Enzymatically active defatted material obtained from 1,500 mg. whole fresh liver and stomach.

***Enzymatically active defatted material obtained from 750 mg. of whole fresh pancreas.

Dosage: 3 capsules daily, with meals.

Supplied: Bottles of 60 capsules, prescription only.

NEW NEOBON® LIQUID

A GERIATRIC TONIC

Now also available for your consideration is NEOBON LIQUID, which provides hematinic action, improved carbohydrate and protein utilization, gonadal and thyroid hormone supplementation and a mild antidepressant action.

The pleasant tasting liquid is especially indicated when a combined attack against nutritional, physiological and mental depression is indicated. Each teaspoonful (5 cc.) of pleasant-tasting NEOBON LIQUID contains:

Ferrous Gluconate	30 mg.
Ascorbic Acid	50 mg.
d-Amphetamine Sulfate	0.5 mg.
Folic Acid	167 mcg.
Vitamin B_{12}	2.5 mcg.
l-Thyroxine	0.1 mg.
Ethinyl Estradiol	1 mcg.
Methyltestosterone	1 mg.
Liver Fraction I	25 mg.
Ethyl Alcohol	0.5 cc.

Dosage: One teaspoonful twice daily before meals, or as required.

Supplied: In 16 fluid ounce bottles, prescription only.

Bibliography

1. Anonymous. 2. Rosenthal, P.: Geriatrics 10:382 (August) 1955. 3. Lansing, A. I.: Symposium on Problems of Gerontology, National Symposium Series No. 9 (August) 1954. 4. Mason-Hohl, E.: Quoted in W. Va. Med. J. 51:16 (January) 1955. 5. Rosenberg, H. R., et al.: Arch. Biochem. and Biophys. 49:263, 1954. 6. Bricker, M., Mitchell, H. H. and Kinsman, G. M.: J. Nutrition 30:269, 1945. 7. Masters, W. H. and Bailey, J. W.: Geriatrics 10:1, 1 (January) 1955.

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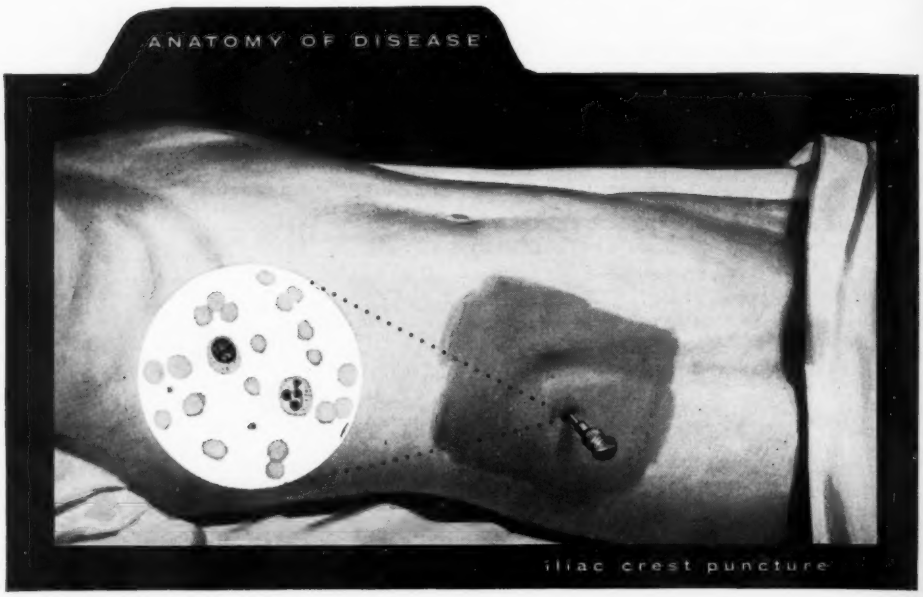


now . . . for better patient response
all factors to treat **all** treatable anemias

ARMATRINSIC

One of the reasons for better patient response . . . Armatrinsic supplies ferrous betainate hydrochloride—the new iron salt with the "built-in" hydrochloric acid, important for proper iron absorption.

JUST 1 ARMATRINSIC CAPSULE B.I.D. SUPPLIES:

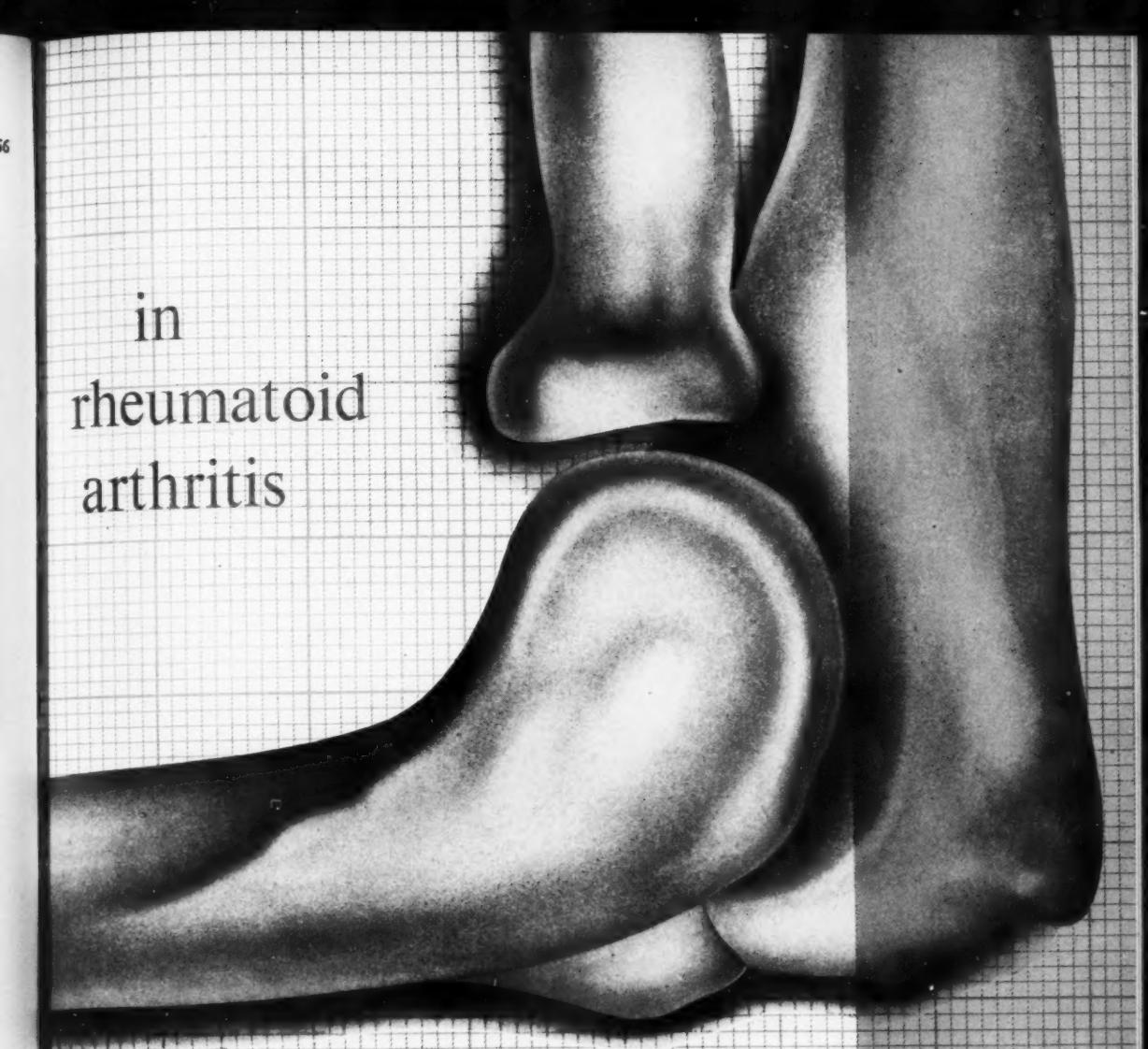
Vitamin B_{12} with Intrinsic Factor Concentrate*	1 U.S.P. Unit (Oral)
Liver Fraction 2 N.F. with Duodenum (Containing Intrinsic Factor)	100 mg.
Vitamin B_{12} Activity Concentrate	10 mcg.
Ferrous Betainate HCl equivalent to 100 mg. of Elemental Iron 18 cc. of N/10 HCl	606 mg.
Folic Acid	1.4 mg.
Ascorbic Acid U.S.P.	100 mg.
Cobalt Chloride	.30 mg.
Molybdenum	1.5 mg.
Copper	0.50 mg.
Manganese	0.50 mg.
Zinc	0.50 mg.

*Unitage established before compounding

Adults: 2 or 3 capsules daily with meals.
Bottles of 50 capsules (small, attractive, odorless)

. . . and for your anemic patients who prefer *liquids* **ARMATINIC® *Liquid***
For a fast start and vigorous improvement
Bottles of 8 and 16 fl.oz.

THE ARMOUR LABORATORIES
A DIVISION OF ARMOUR AND COMPANY • KANKAKEE, ILLINOIS



in
rheumatoid
arthritis

replaces cortisone and hydrocortisone
permits treatment of more patients

METICORTEN*

(PREDNISONE, SCHERING)

Schering

- significantly less edema due to sodium retention
- excellent relief of pain, swelling, tenderness
- effective in smaller dosage

*T.M.

MC-J-53-1255

touch and

in dermatitis due to

brand of oxytetracycline and hydrocortisone

topical ointment

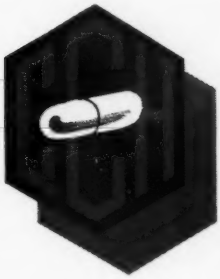
"considered the choice in secondarily infected dermatoses and those in which secondary infection is known to be a frequent complication."[1]

Supplied: In 1 2 oz. tubes containing 3% oxytetracycline hydrochloride (TERRAMYCIN®) and 1% hydrocortisone (CORTRIL®) in a specially formulated, easily applied base.

Pfizer

Division, Chas. Pfizer & Co., Inc., Brooklyn 6, New York

1. Leeder, E. E.: M. Times 83:1259, 1955.



FOR NEARLY 20 YEARS

HASKELL'S

BELBARB

has provided Safe, Effective Spasmolysis and Sedation

NOW IN 5 CONVENIENT DOSAGE FORMS

	Phenobarbital	Belladonna Alkaloids	Supplied
1 BELBARB No. 1 per tablet	¼ gr.	hyoscyamine, atropine, and scopolamine in fixed proportion, approximately equivalent to Tr. Belladonna, 8 min.	Bottles of 100, 500 and 1,000 tablets
2 BELBARB No. 2 per tablet	½ gr.		Bottles of 100, 500 and 1,000 tablets
3 BELBARB-B with B Complex Supplement*	¼ gr.		Bottles of 100, 500 and 1,000 tablets
4 BELBARB Elixir per fluidrachm (4 cc)	¼ gr.		Bottles containing 1 pt. and 1 gal.
5 BELBARB Trisules	1 Trisule is equivalent to 3 Belbarb tablets		Bottles of 30 and 100 Trisules

*Thiamine Hydrochloride — 5 mg., Riboflavin — 2 mg., Calcium Pantothenate — 2.5 mg., Pyridoxine Hydrochloride — 0.5 mg., Niacinamide — 10 mg., Vitamin B_{12} Activity — 2 mcg.

Send for free samples and literature.

CHARLES C. HASKELL & CO., INC., Richmond, Virginia

THORAZINE* *can help your patients to endure the suffering caused by* ***severe pain***

for example: ***in burns***

Thorazine's ataraxic, tranquilizing action can reduce the suffering caused by the pain of severe burns. 'Thorazine' acts, not by eliminating the pain, but by altering the patient's reaction—enabling him to view his pain with what has been described as "serene detachment." Karp et al.,[1] reporting on the use of 'Thorazine' in patients with severe pain, observed that 'Thorazine' produced "a quiet, phlegmatic acceptance of pain."

It is obvious that not all cases of severe pain are suitable for 'Thorazine' therapy. 'Thorazine' is most useful when the psychic element is important.

'Thorazine' is available in ampuls, tablets and syrup (as the hydrochloride), and in suppositories (as the base).

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

1. Karp, M., et al.: Am. J. Obst. & Gynec. 69:780 (April) 1955.

Quickly Relieves Nasal Congestion in Colds, Sinusitis, Allergic Rhinitis

contains:

Phenylephrine Hydrochloride 0.15%
"Propadrine" Hydrochloride 0.3%
In an isotonic saline menstruum

RHINALL *nose drops*

A better nasal medication to assure your patient of prompt, prolonged relief.

- Safe for children and adults
- No burning or irritation
- No bad taste or after-reactions
- No risk of sensitization

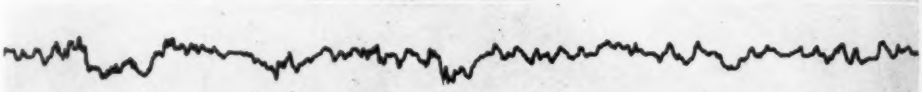
Same proven formula available in ½ oz. plastic spray bottle. Samples on request.

RHINOPTO COMPANY, DALLAS, TEXAS

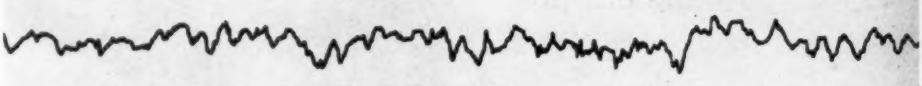
Ethical Specialties for the Profession

WHAT IS THE DIFFERENCE BETWEEN A TRANQUILIZER AND A SEDATIVE?

Comparison of the effect of Raudixin (tranquilizer) and a barbiturate (sedative) on the cortical electroencephalogram



No drug.



After Raudixin. E. E. G. not altered.

After barbiturate. Typical "spindling" effect.

Because barbiturates and other sedatives depress the cerebral cortex, the sedation achieved is accompanied by a reduction in mental alertness.

Raudixin acts in the area of the midbrain and diencephalon, and does not depress the cerebral cortex. Consequently, the tranquilizing (ataractic) effect achieved is generally free of loss of alertness.

RAUDIXIN

Squibb Whole Root Rauwolfia Serpentina

DOSAGE: 100 mg. b.i.d. initially; may be adjusted within a range of 50 mg. to 500 mg. daily. Most patients can be adequately maintained on 100 mg. to 200 mg. per day.

SUPPLY: 50 mg. and 100 mg. tablets; bottles of 100, 1000 and 5000.

SQUIBB *Squibb Quality—the Priceless Ingredient*

*RAUDIXIN® IS A SQUIBB TRADEMARK

new

Azo Gantrisin

Especially for Urinary Tract Infections

Azo Gantrisin provides -- in a single tablet -- the wide antibacterial spectrum of Gantrisin plus the local pain-relieving action of a widely accepted urinary tract analgesic.

Advantages of Azo Gantrisin: Effective antibacterial concentrations in blood as well as urine; prompt relief of local discomfort; rapid appearance of orange-red dye in urine also has favorable psychologic effect.

Each tablet contains 0.5 Gm Gantrisin 'Roche' plus 50 mg phenylazo-diamino-pyridine HCl.

Hoffmann - La Roche Inc
Nutley · N.J.

ROCHE

Gantrisin® - brand of sulfisoxazole

For patients who take their troubles to bed —

Noludar 'Roche' brings welcome rest. Not a barbiturate, not habit forming, 200 mg induces a sound night's sleep without hangover, or 50 mg t.i.d. provides daytime sedation without somnolence.

Noludar tablets, 50 and 200 mg; elixir, 50 mg per teaspoon.

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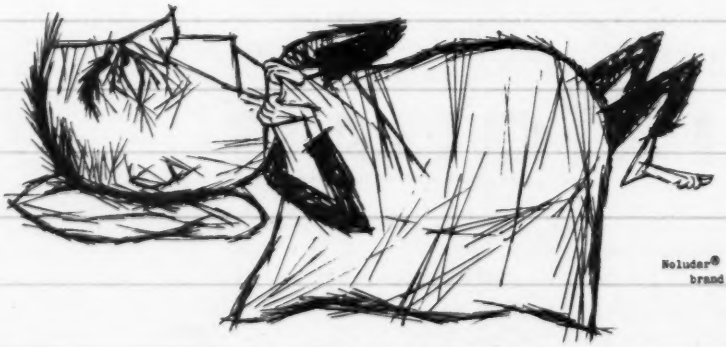
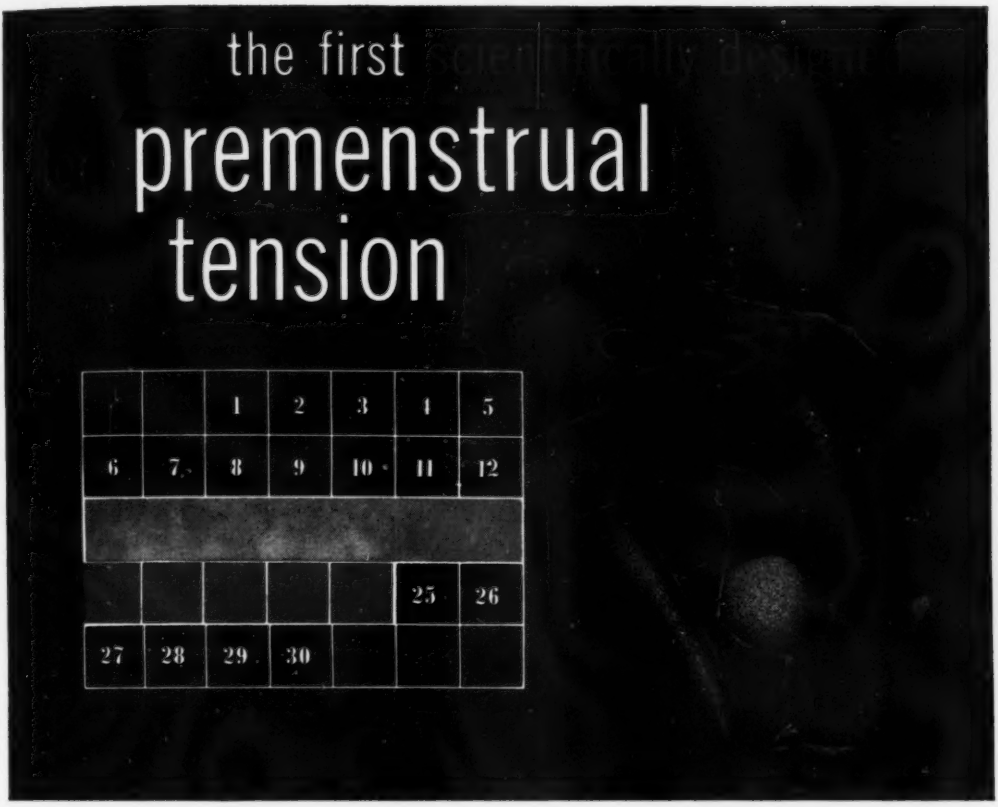
Nutley 10, New Jersey



Noludar®
brand of methyprylon



neo Bromth®

Brand of Bromaleate, Brayten

NEO BROMTH, the first preparation developed specifically for treatment of premenstrual tension, continues to be found the most satisfactory therapeutic agent in this condition.

Bickers found that "abnormal water storage can be blocked or eliminated and clinical relief of symptoms obtained in most patients . . ."[1] with NEO BROMTH.

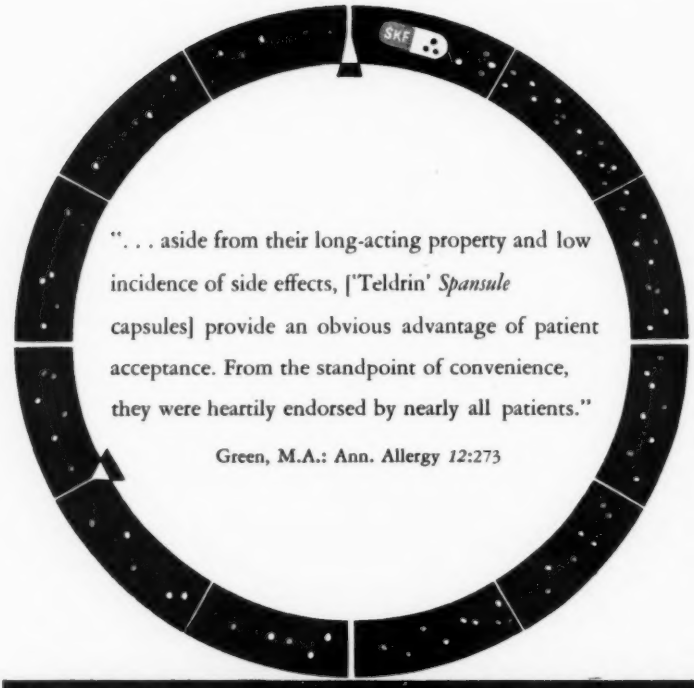
Greenblatt recently stated: "Clinically, we share Bickers' enthusiasm for this drug in the management of premenstrual tension, especially where there is associated edema."[2]

NEO BROMTH is non-toxic, *non-hormonal* therapy and contains no ammonium chloride. Each 80 mg. tablet contains 50 mg. of pamabrom (2-amino-2-methyl-1-propanol 8 bromo-theophyllinate) and 30 mg. of pyrilamine maleate.

Dosage: 2 tablets twice daily (morning & night) beginning at onset of symptoms —usually 5 to 7 days before menses. Discontinue at onset of flow. Supplied in bottles of 100 tablets on prescription only.

1. Bickers, W.: Southern M.J., 46:873, Sept., 1953
2. Greenblatt, R.: GP, 11:66, March, 1955

BRAYTEN PHARMACEUTICAL COMPANY Chattanooga 9, Tennessee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". . . aside from their long-acting property and low incidence of side effects, ['Teldrin' *Spansule* capsules] provide an obvious advantage of patient acceptance. From the standpoint of convenience, they were heartily endorsed by nearly all patients."
Green, M.A.: Ann. Allergy *12*:273

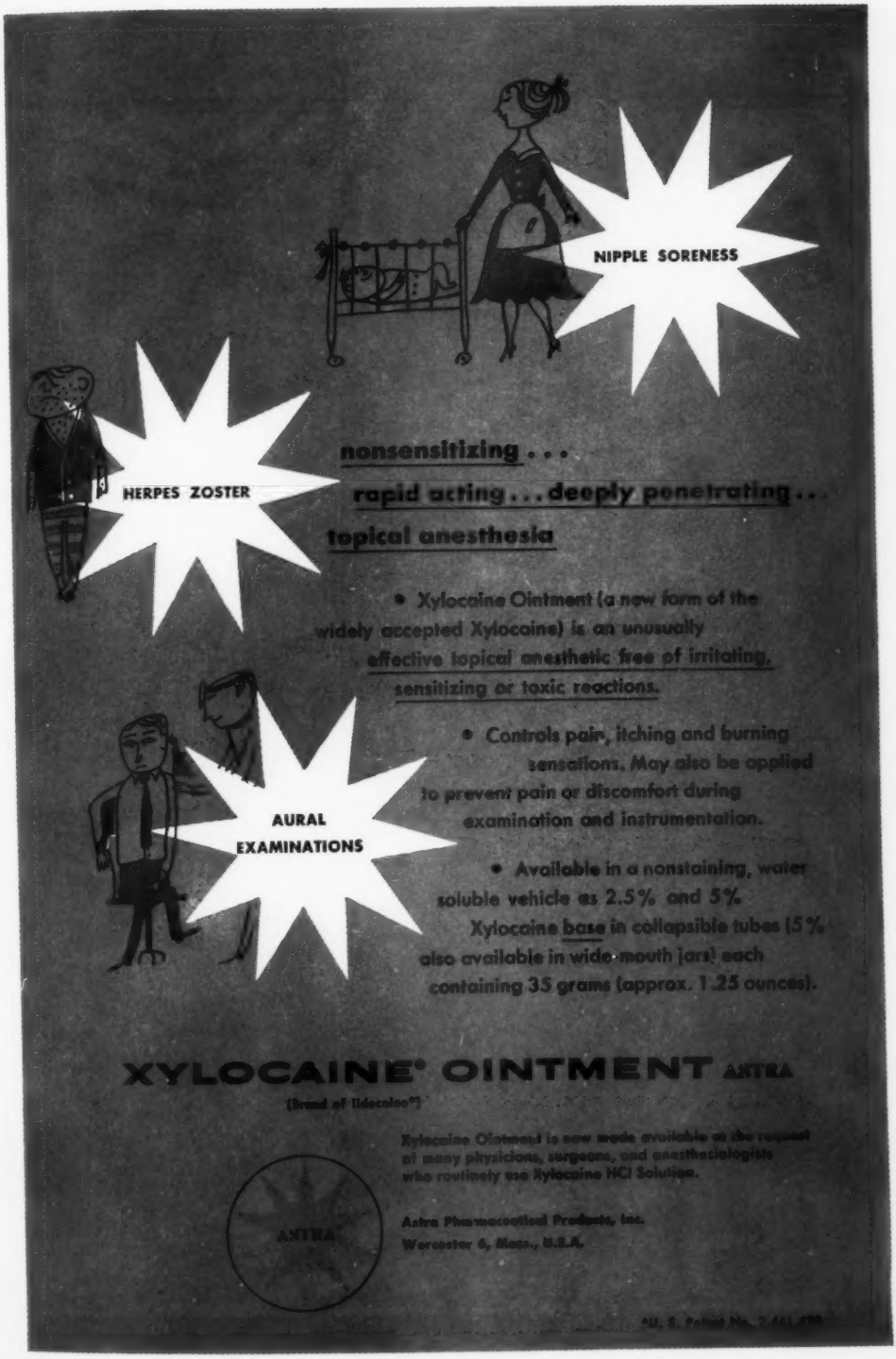
24-hour continuous allergic protection with a single capsule q12h

Teldrin*
chlorprophenpyridamine maleate
Spansule*
sustained release capsules, S.K.F.
Antihistamine

8 mg. & 12 mg.

made only by
Smith, Kline & French Laboratories, Philadelphia
first in sustained release oral medication

*T.M. Reg. U.S. Pat. Off. Patent Applied For



nonsensitizing . . .
rapid acting . . . deeply penetrating . . .
topical anesthesia

• Xylocaine Ointment (a new form of the widely accepted Xylocaine) is an unusually effective topical anesthetic free of irritating, sensitizing or toxic reactions.

• Controls pain, itching and burning sensations. May also be applied to prevent pain or discomfort during examination and instrumentation.

• Available in a nonstaining, water soluble vehicle as 2.5% and 5% Xylocaine base in collapsible tubes (5% also available in wide-mouth jars) each containing 35 grams (approx. 1.25 ounces).

XYLOCAINE® OINTMENT ASTRA

(Brand of lidocaine*)

Xylocaine Ointment is now made available at the request of many physicians, surgeons, and anesthesiologists who routinely use Xylocaine HCl Solution.

ASTRA

Astra Pharmaceutical Products, Inc.
Worcester 6, Mass., U.S.A.

*U. S. Patent No. 2,441,498

now... treatment on **two** therapeutic levels important in hypertension

HOW UNITENSEN WITH RESERPINE LOWERS BLOOD PRESSURE

1 BLOOD PRESSURE

patient	C.M.	A.T.	G.R.	B.S.	N.F.	R.G.	V.F.
age	34	65	77	62	58	51	41
Smithwick group	4	3	4	3	3	3	4
Blood Pressure BEFORE	195/130	205/115	210/130	250/115	220/130	205/110	215/120
Blood Pressure AFTER	160/95	175/110	170/96	170/95	175/105	180/90	175/100

(from Cohen, Cross & Johnson: Am. Pract. 6: 1030, 1955.)

2 PSYCHE

"The symptoms of hypertension usually arise in a social setting of emotional stress."[1] Unitensen-R helps to calm down the hypertensive patient and make him feel better.

1. Weiss, E.: Am. Pract. 6: 1680, 1955.

Unitensen-R combines Unitensen—a safe, effective anti-hypertensive agent and reserpine—a tranquilizing alkaloid of rauwolfia. Unitensen-R dependably lowers blood pressure in most patients without serious side effects; and at the same time, gives patients a feeling of well-being. Dosage is simple and tablets are economical.

UNITENSEN*-R TABLETS

*T.M. Reg., U.S. Pat. Off.

Each Unitensen-R tablet contains:

Cryptenamine (as tannate salt)	1 mg.
Reserpine	0.1 mg.

Bottles of 50, 100, 500 and 1000.

***Also available:** Unitensen Tannate Tablets brand of cryptenamine*

IRWIN, NEISLER & COMPANY • DECATUR, ILLINOIS

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MEDICAL SCHOOL AND HOSPITAL

(ORGANIZED 1881)

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COURSE for GENERAL PRACTITIONERS

Intensive full-time instruction covering those subjects which are of particular interest to the physician in general practice. Fundamentals of the various medical and surgical specialties designed as a practical review of established procedures and recent advances in medicine and surgery. Subjects related to general medicine are covered and the surgical departments participate in giving fundamental instruction in their specialties. Pathology and radiology are included. The class is expected to attend departmental and general conferences.

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A two-months combined surgical course comprising general surgery, traumatic surgery, abdominal surgery, gastroenterology, proctology, gynecological surgery, urological surgery. Attendance at lectures, witnessing operations, examination of patients pre-operatively and post-operatively and follow-up in the wards post-operatively. Pathology, radiology, physical medicine, anesthesia. Cadaver demonstrations in surgical anatomy, thoracic surgery, proctology, orthopedics. Operative surgery and operative gynecology on the cadaver; attendance at departmental and general conferences.

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A comprehensive review of the physics and higher mathematics involved, film interpretation, all standard general roentgen diagnostic procedures, methods of application and doses of radiation therapy, both X-ray and radium, standard and fluroscopic procedures. A review of dermatological lesions and tumors susceptible to roentgen therapy is given, together with methods and dosage calculation of treatments, special attention is given to the newer diagnostic methods associated with the employment of contrast media such as bronchography with Lipiodol, uterosalpingography, visualization of cardiac chambers, perirenal insufflation and myelography. Discussions covering roentgen departmental management are also included; attendance at departmental and general conferences.

PRACTICAL ELECTROCARDIOGRAPHY

A two-weeks part time elementary course for the practitioner based upon an understanding of electrophysiologic principles. Standard, unipolar and precordial electrocardiography of the normal heart. Bundle branch block, ventricular hypertrophy and myocardial infarction considered from clinical as well as electrocardiographic viewpoints. Diagnosis of arrhythmias of clinical significance will be emphasized. Attendance at, and participation in, sessions of actual reading of routine hospital electrocardiograms.

For Information about these and other courses Address

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Impressive Response
In the Acutely Agitated Patient...

- The acute alcoholic
- The acute psychotic
- The drug addict

The **NEW** Phenothiazine Derivative

Supplied: Tablets, 25, 50, and 100 mg., bottles of 50 and 500; 200 mg., bottles of 500. Injection, 50 mg. per cc., vials of 2 and 10 cc.

Sparine* HCl

Promazine Hydrochloride

10-(γ-dimethylamino-n-propyl)-phenothiazine hydrochloride

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An Exclusive Development of Wyeth Research

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"the gratitude of the patient is ample reward"...

"Vaginal discharge is a common complaint amongst women of all ages ... this is one of the conditions in which the gratitude of the patient is ample reward for the time and trouble spent in treatment," states one investigator. Gantrisin Vaginal Cream is highly effective against many sulfonamide-susceptible microorganisms which are frequently found in vaginal and cervical infections. Its acid pH of 4.6 promotes the return of the flora found in a healthy vagina.

Gantrisin®-- brand of sulfisoxazole

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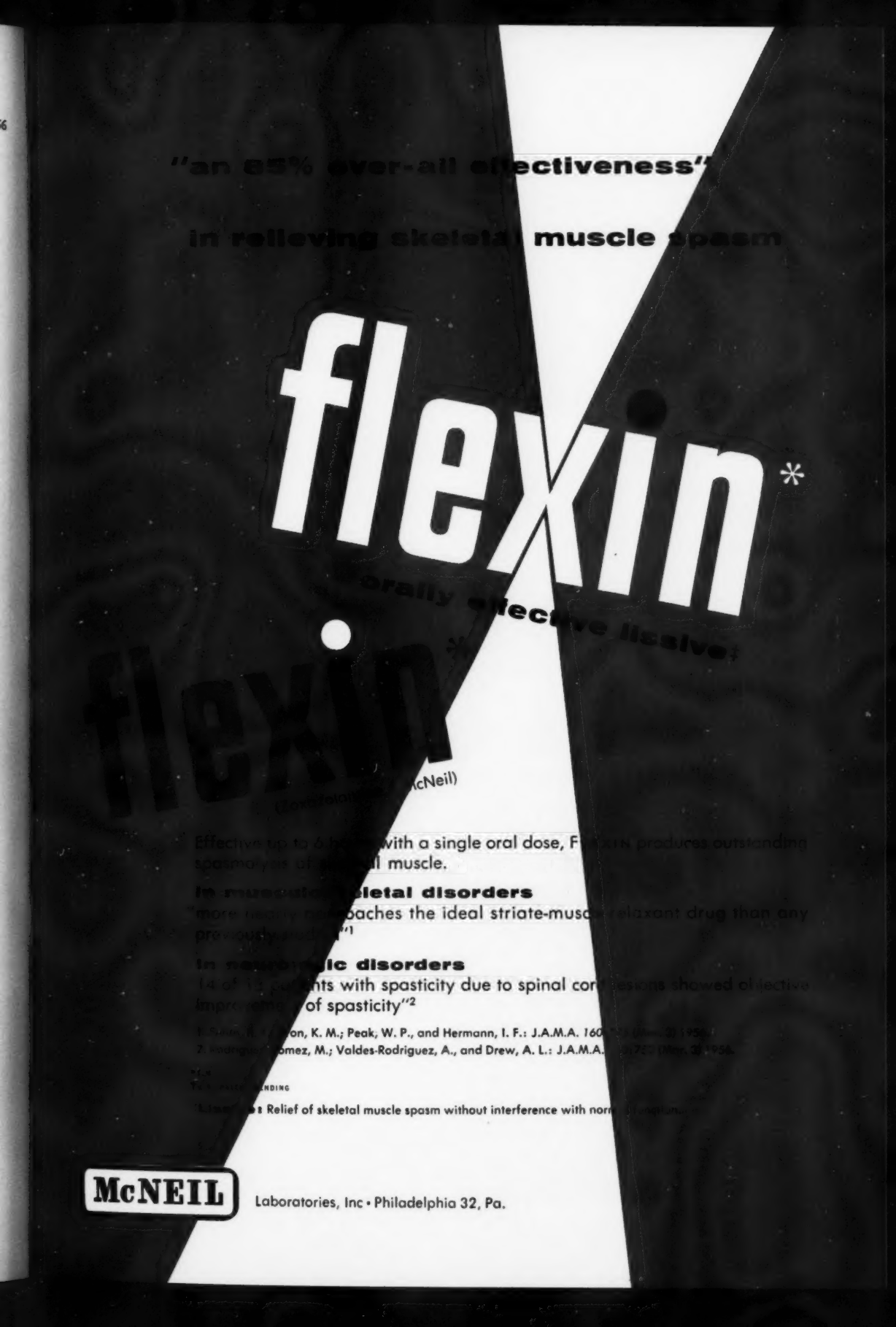
"an 85% over-all effectiveness"
in relieving skeletal muscle spasm
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orally effective lissive
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with a single oral dose, F
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baches the ideal striate-musc
relaxant drug than any
"[1]
ic disorders
nts with spasticity due to spinal cor
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of spasticity"[2]
on, K. M.; Peak, W. P., and Hermann, I. F.: J.A.M.A. 160
omez, M.; Valdes-Rodriguez, A., and Drew, A. L.: J.A.M.A.
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often succeeds
in stubborn
skin conditions
unresponsive to
other therapy

PANTHO-F CREAM

HYDROCORTISONE	1%
PANTOTHENYLOL	2%

in a water-miscible, pleasant, stainless, vanishing cream base; virtually non-sensitizing

. . . provides the dramatic anti-inflammatory action of hydrocortisone alcohol
. . . plus the anti-pruritic and healing power of pantothenylol, the active ingredient of Panthoderm Cream.

new, decisive advance in topical hydrocortisone therapy

PANTHO-F CREAM

rapidly allays inflammation
relieves pain, itch, swelling
checks oozing and edema
promotes smooth granulation
accelerates healing

in
eczemas (infantile, lichenified, etc.)
dermatitis (atopic, contact, eczematoid)
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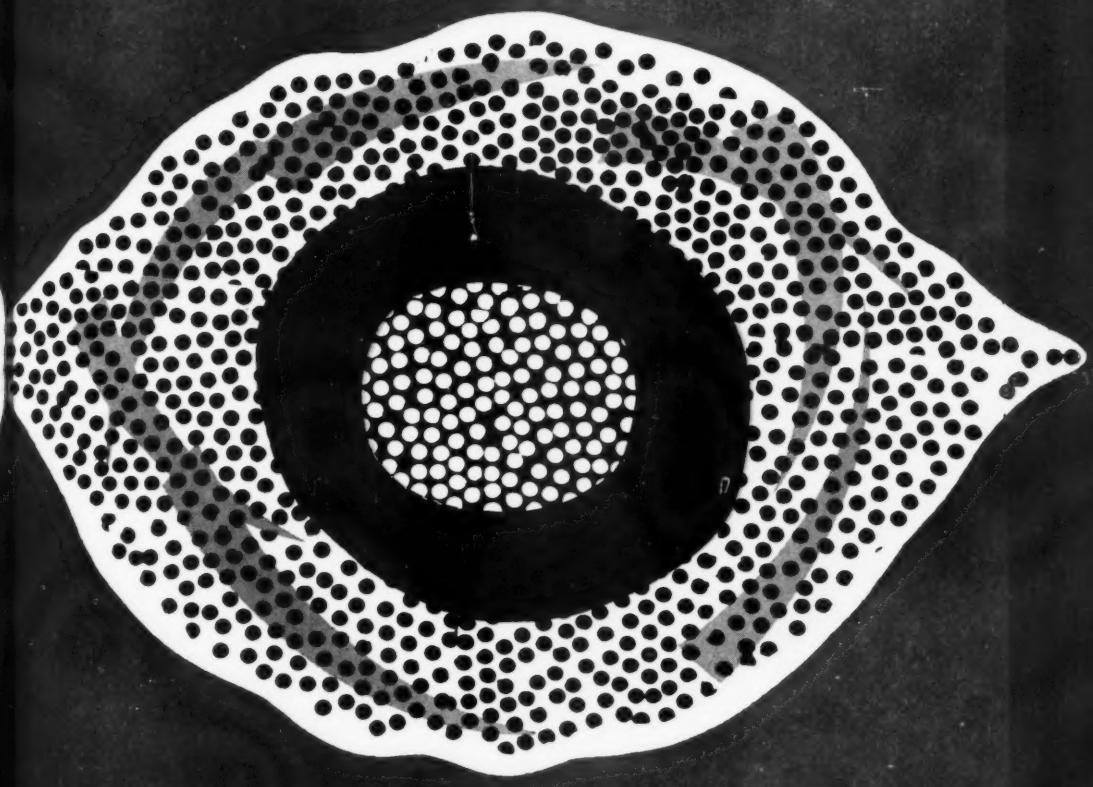

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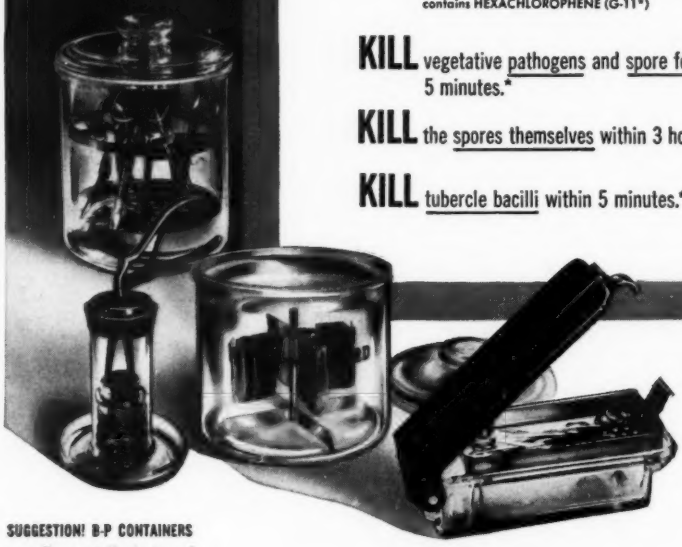

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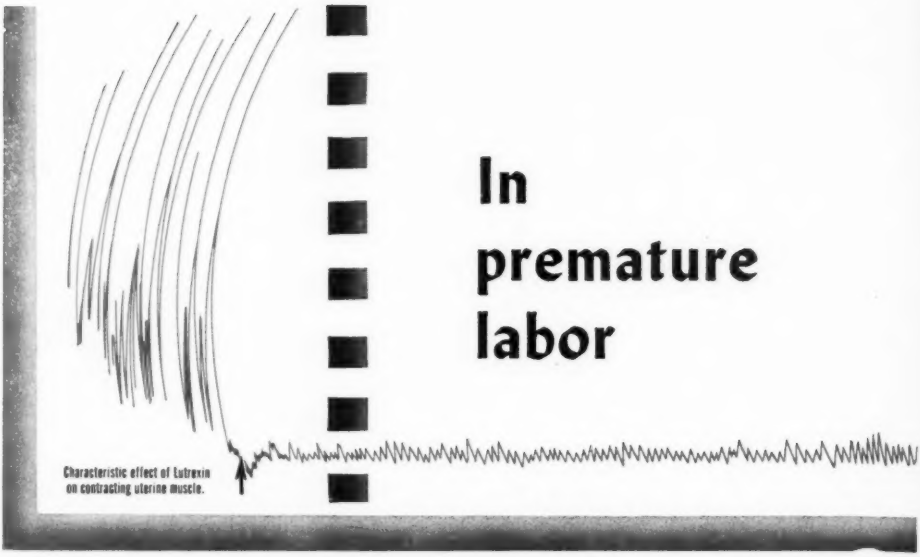

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Southern Medical Journal

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The L. E. Test in Patients Presenting the Clinical Picture of Rheumatoid Arthritis*

S. WILLIAM ROSS, M.D., *Little Rock, Ark.*, and
E. K. CLARDY, M.D.,† *Hot Springs, Ark.*

The specificity of the L. E. cell for disseminated lupus is questioned in some quarters. Therefore it is difficult to evaluate the significance of the L. E. cell in rheumatoid arthritis and particularly after the use of cortisone and its discontinuance.

SINCE HARGRAVES'[1] INITIAL DESCRIPTION of the L. E. cell phenomenon, considerable general interest has been shown in systemic lupus erythematosus (S. L. E.). Using this test as the principal criterion for the diagnosis, many clinical syndromes hitherto considered diagnostic problems have been identified as examples of S. L. E. In this country various groups having appreciable experience with the L. E. test supported the validity of this procedure as a diagnostic aid. During the past few years, however, there have been several reports involving a relatively small group of patients in whom so-called false positive L. E. tests were observed. The diseases represented by this group included multiple myeloma,[2] pernicious anemia,[3] discoid lupus erythematosus,[3] fungus disease[4] or contamination,[5] Senear-Usher pemphigus,[6] miliary tuberculosis,[7,8] dermatitis herpetiforms,[3] leukemia,[9] as well as reaction to certain drugs including penicillin,[10] hydralazine,[11] and hydantoin.[12] Meyler[13] reported leukophagocytosis and erythrophagocytosis but no L. E. cells in tests on patients with allergic reactions to various drugs. As a result of these reports a reevaluation of the significance and interpretation of the L. E. cell phenomenon has seemed indicated. However, this poses several problems. As Harvey and associates[14] have pointed out, systemic L. E. cannot be accurately and consistently identified. The pathologic lesions are somewhat variable in their occurrence and no one of them is specific. Since the advent of the L. E. test there has been a tendency to attribute most all other unexplained findings in a patient with a positive test to systemic L. E. In the same manner, after a positive test is obtained, there is a propensity to interpret minor changes as significant ones. With this in mind one must conscientiously inquire whether or not the L. E. test is coincident to some of the manifestations reported to occur in systemic L. E. and whether or not some of these abnormalities may occur just as frequently in a control group of sick patients with negative L. E. tests. It is this latter problem that we decided to approach.

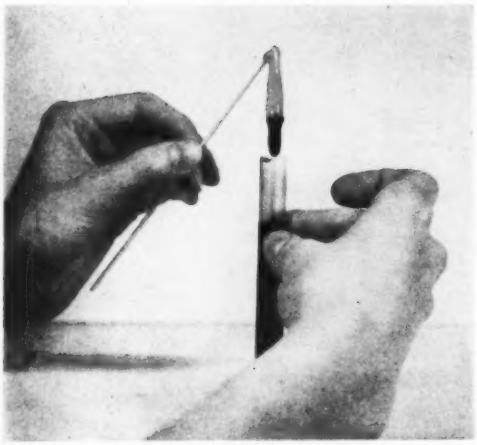
Clinical Study

In our study we selected patients with rheumatoid or rheumatoid-like arthritis. We proposed to determine if there was any correlation between the L. E. test and features of systemic lupus erythematosus other than the rheumatoid picture. During the past 10 months, 79 patients who presented the findings of rheumatoid or rheumatoid-like arthritis were examined. In each case the physician who took the initial history and did the physical examination was unaware of the outcome of the L. E. test on the patients.

*Read before the Section on Medicine, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

†From the Department of Medicine, University of Arkansas School of Medicine, Little Rock, Ark., and the Leo N. Levi Memorial Hospital, Hot Springs, Ark.

FIG. 1



The clot is picked up with a wooden applicator stick. The serum end of the clot is above, the packed red cells below and the buffy layer is found at the line of demarcation between the two.

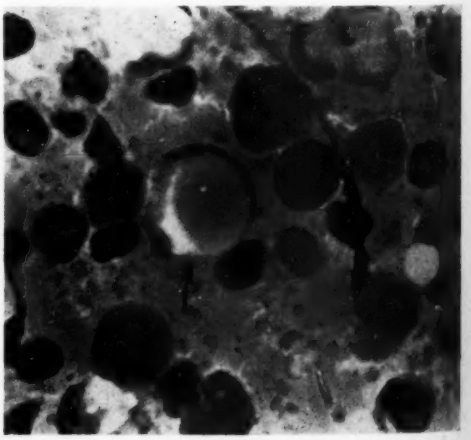
The joint involvement was graded according to the classification recommended by the American Rheumatism Association[15] and the findings indicative of multisystem involvement were recorded. The minimal accepted physical findings were heat and swelling in at least one joint. In addition certain routine laboratory examinations were incorporated in the analysis. These included a complete blood count, erythrocyte sedimentation rate, urinalysis, serologic test for syphilis, total protein and fractionation, electrocardiogram, and chest x-ray study. Appropriate tests were performed where there was any suggestion of other system involvement.

The L. E. cell test was carried out by two methods, one using an anticoagulant according to a modification of the method of Mathis,[16] and a second using no anticoagulant, a modification of the method of Zimmer and Hargraves.[17] The method for the L. E. test without anticoagulant is as follows:

1. Seven cc. of venous blood are drawn into a dry syringe, placed immediately into a clean, dry test tube and centrifuged within one minute at 2,000 r.p.m. for 10 minutes.
2. Blood is incubated at room temperature for one hour. At this stage the clot appears in two layers with serum above and packed cells below.
3. The serum end of the clot is picked up with forceps or applicator sticks (Fig. 1).
4. Scissors are used to cut the clot one-fourth inch below and one-fourth inch above the serum-red cell boundary.
5. The center one-half inch which contains the buffy layer is placed in a small beaker and teased out with wooden applicator sticks.
6. The fluid portion is aspirated with a capillary pipette and placed in a Wintrobe hematocrit tube, the fluid volume usually being just sufficient to fill the tube.
7. This is centrifuged at 2,000 r.p.m. for 10 minutes and then incubated at 37° C. for one hour.
8. The serum portion is removed and the buffy layer aspirated. Smears of the latter are made on cover slips, stained with Wright's stain and mounted on glass slides.

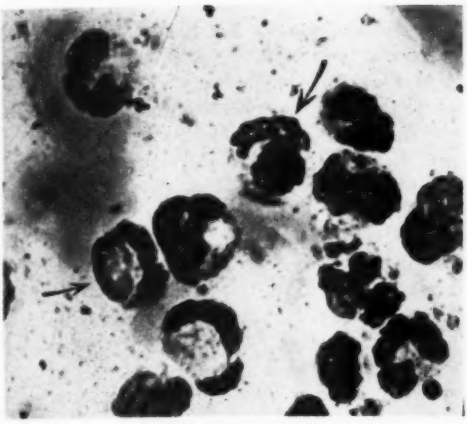
Each L. E. test was done twice on each patient usually with a week's interval. These slides were identified solely by numbers and were read by one individual to whom no clinical information was supplied. To further prevent bias, miscellaneous slides were included. Because in this study there were so few positive L. E. tests, we analyzed patients from the University Hospital who had been examined in the last 5 years, who fit the above criteria and who had had positive L. E. cell tests. In each of the latter cases the examining physician had no prior knowledge of the

FIG. 2



Arrow points to a typical L. E. cell.

FIG. 3

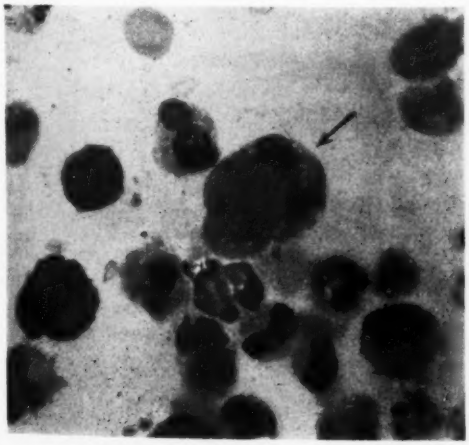


Arrows point to tart cell.

results of the L. E. test. Other findings were added only if there was unequivocal evidence, laboratory or clinical, to corroborate them. Twelve cases were obtained. At the conclusion of the study the L. E. tests were correlated with the clinical summaries.

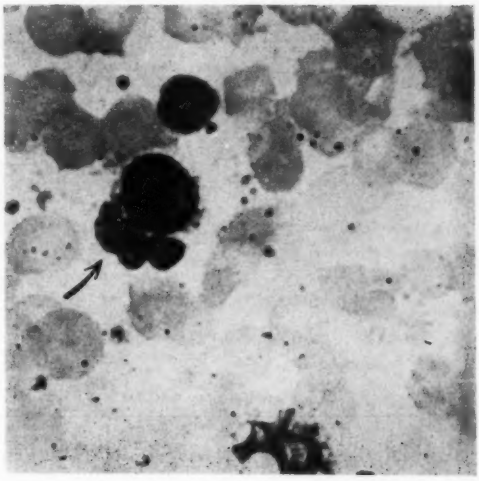
The criteria we used in the identification of an L. E. cell are depicted in figure 2, which represents an L. E. cell from one of the patients in this group. It is characteristically a neutrophilic polymorphonuclear leukocyte containing an ingested mass of homogeneous, purple staining material. The color of the engulfed mass may vary from smokey blue to pink but must be without remnants of nuclear structure. Figure 3 reveals a similar cell in

FIG. 4



Arrow points to an advanced tart cell.

FIG. 5



Arrow points to an advanced tart cell.

which a moderate amount of nuclear structure remains in the ingested nuclear mass. Hargraves[1] designated this a tart cell. It is without diagnostic significance. Figures 4 and 5 demonstrate what Weiss and Swift[18] have called an advanced tart cell. The advanced tart cell may be found in positive L. E. preparations but also may occasionally appear in the blood of patients with other diseases. It is important, therefore, to differentiate it from a true L. E. cell. In all of our tests more than one typical L. E. cell was identified before the L. E. phenomenon was considered present.

Results

Because the basis of admission to the two hospitals is different we handled the data separately. There were no L. E. positive patients in the Leo N. Levi Memorial Hospital group. Table 1 illustrates the distribution of patients according to the aforementioned rheumatoid classification. By *stage,* it refers to the degree of advancement of the disease, by *class* to the functional capacity of the patient, and by *grade* to the degree of activity of the disease. In each group, the Roman numerals I through IV indicate increasing severity. In the Levi Hospital group a greater proportion of patients exhibited the more advanced stages of joint involvement, whereas in the L. E. positive group at the University Hospital there was a tendency to less marked

TABLE 1

DISTRIBUTION OF PATIENTS ACCORDING TO CLASSIFICATION OF JOINT INVOLVEMENT*

		Stage	Class	Grade
University Hospital				
L. E. Positive	I	8	0	0
	II	5	9	0
	III	4	5	6
	IV	1	4	12
L. E. Negative	I	6	1	0
	II	4	8	2
	III	7	7	8
	IV	3	4	10
Levi Hospital				
L. E. Negative	I	6	7	0
	II	7	22	11
	III	25	19	34
	IV	15	5	8

*As recommended by the American Rheumatism Association.

joint changes. The activity of disease was less intense in the Levi Hospital group.

Table 2 reflects the number of patients who manifested involvement in each system. The numerators represent those findings which are known to occur in S. L. E. Since some of the abnormalities were found to be associated with coexistent disease, we felt that these figures were somewhat misleading. We, therefore, modified the results by eliminating those findings which appeared most likely the consequence of a concurrent disease. These results are tabulated in the denominators. Minor electrocardiographic aberrations unsupported by the clinical picture were deleted. Changes such as leukocytosis and moderate anemia, commonly found in both diseases, were not enumerated. In that the constitutional and skeletal changes as well as the presence of subcutaneous nodules were considered in the rheumatoid classification they are disregarded here. In no instances were symptoms included if they could not be verified by objective laboratory or physical findings. In general there are more nonspecific findings included in the L. E. negative groups. For example most of the skin changes in the L. E. positive group were suggestive or characteristic of L. E. by clinical or pathologic examination, whereas in the L. E. negative group purpura and drug reactions accounted for more than half of the changes. Nevertheless, it may be observed that there is a markedly higher frequency of involvement within each system in the L. E. positive group whether the comparison is made on the basis of the uncorrected figures in the numerators or the more pertinent figures in the denominators.

TABLE 2

NUMBER OF PATIENTS REVEALING INVOLVEMENT BY SYSTEMS

	Total Cases	C.V.	Pul.	Renal.	G.I.	R.E.	Nerv.	Skin & M.M.	Eye
University Hospital									
L. E. Positive	18/18	11/11	13/11	16/16	15/14	13/13	9/8	13/13	4/4
L. E. Negative	20/20	4/3	7/2	4/2	4/2	2/1	2/2	8/7	0/0
Levi Hospital									
L. E. Negative	53/53	5/2	4/3	2/1	1/0	0/0	0/0	2/2	0/0

C. V.—Cardiovascular
Pul.—Pulmonary
G.I.—Gastrointestinal
R. E.—Reticuloendothelial
Nerv.—Nervous
M. M.—Mucous membranes

Numerators represent abnormalities consistent with S. L. E. found in patients. Denominators represent these figures after findings associated with coexistent disease are deleted.

As an example of the deletions in the University Hopsital L. E. negative group; one patient had thyrotoxicosis with cardiac failure and leukopenia; five had fibrocalcific disease radiographically; one had chronic pyelonephritis; one had a trace of albumin; two had gallbladder disease; and one had psoriasis.

Table 3 demonstrates a clearly greater degree of multisystem involvement in each patient in the L. E. positive group when compared to the L. E. negative groups. Again the numerators represent the number of patients in whom all the abnormalities consistent with S. L. E. are considered. The denominators reflect the number of patients after the findings associated with coexistent disease are eliminated from the tabulation. In the L. E. positive group 15 of 18 patients revealed abnormalities in four or more systems whereas 17 of 20 in the University Hospital and 45

TABLE 3

DISTRIBUTION OF PATIENTS ACCORDING TO NUMBER OF SYSTEMS INVOLVED

University Hospital	Total Cases	Number of Systems 0	1	2	3	4	5	6	7	8
L. E. Positive	18/18	0/0	0/0	0/0	2/2	5/7	6/4	1/1	1/2	3/2
L. E. Negative	20/20	6/10	7/7	2/1	3/1	1/0	1/1	0/0	0/0	0/0
Levi Hospital										
L. E. Negative	53/53	39/45	13/8	1/0						

Patients in numerators and denominators correspond to the findings in the numerators and denominators, respectively of table 2.

of 53 in the Levi Hospital had one or no systems affected. There was only one patient in either L. E. negative group who had more than three systems involved. This patient had a hemolytic anemia, leukopenia, hepatosplenomegaly and albuminuria. She had been on cortisone or comparable steroid for one and one-half years. In none of the groups was there evident correlation between the number of patients showing involvement of each system and the rheumatoid classification nor between the latter and the number of systems involved in each patient.

Discussion

Recently Weiss and Swift[18] discussed the so-called "false positive" cases reported in the literature. In general we concur with their interpretation,—namely that many of these can be explained in other ways.

1. Criteria for identification of the L. E. cell may not have been rigidly maintained as recommended by Hargraves.[1]
2. S. L. E. may actually have been present prior to administration of drugs such as penicillin.
3. Instances following drugs as hydralazine may actually induce cases of S. L. E.
4. S. L. E. may coexist with a disease which masks it clinically.
5. In multiple myeloma the inclusion mass may be an amyloid type of substance.

Jacobs[8] reported positive L. E. tests in a patient with miliary tuberculosis. The patient had a rash following treatment with oral penicillin and again after the use of a sulfonamide. Pigmentation of the skin persisted. She developed a painful swelling of one hand which resolved on hydrocortisone and without antituberculosis therapy. At autopsy, miliary tuberculosis was found but no evidence of S. L. E. This certainly appears to be a well-documented instance of a false positive L. E. test. It is conceivable to us, however, that this patient may well have had two disease processes with one adequately suppressed by therapy so as to reveal no histologic evidence of its presence. McGehee Harvey and associates[14] reported instances of S. L. E. in which there was a surprising lack of histologic change at autopsy, and death was attributed to "chemical" causes.

In contrast to Jacobs' report[8] we observed a 16 year old white girl with the classic features of S. L. E., manifested by a butterfly rash following exposure to the sun, a migratory polyarthritis, pericardial friction rub, pleural effusion, ascites, retinopathy, convulsions, albuminuria, leukopenia and a positive L. E. test. She was treated for a prolonged period with large doses of cortisone and developed pulmonary blastomycosis terminally. On postmortem examination she was found to have marked changes in the lungs due to blastomycosis, but the remainder of the tissues examined showed no evidence of the organism. Also there were no significant histologic changes suggestive of S. L. E. The onset of this patient's disease was 18 months prior to her death. Until four months before death, repeated chest x-ray films revealed normal lung fields. Had the earlier findings been less typical and the course shorter, this case might also have appeared to be one in which there was a false positive L. E. test.

At the present stage of our knowledge it is impossible to state categorically that the clinical and pathologic picture usually found in association with a positive L. E. test represents a distinct and separate disease; neither can we state that it is unrelated to rheumatoid arthritis or to other members of the "collagen" group, nor to discoid lupus erythematosus, glomerulonephritis, nor particular drug reactions. We feel that our study does strongly suggest and support the concept that in patients who reveal evidence of a rheumatoid-like arthritis a positive L. E. test exhibits a high degree of correlation with multisystem disease. From this data we feel secure in recommending that every patient presenting the rheumatoid picture should have an L. E. test. A positive test may forewarn a multisystem disease.

Summary and Conclusions

1. We analyzed 91 patients presenting the features of a rheumatoid-like arthritis according to a standard classification.

2. Eighteen of these patients had a positive L. E. test and revealed a considerably higher incidence of multisystem involvement than did two control groups of 20 and 53 patients with negative L. E. tests.

3. These results uphold the reliability of reports that the incidence of system involve-

ment is related specifically to the positive L. E. tests.

4. The results do not otherwise clarify the relationship of systemic lupus erythematosus to rheumatoid arthritis.

Addendum. Since this paper was written we have collected 17 more cases at the Levi Memorial Hospital. Three of these had positive L. E. tests. This latter group was found to have only one or two systems involved. In one patient the only system involved was the skin. Biopsy revealed changes including hematoxylin bodies compatible with lupus erythematosus. These results do not invalidate our other findings but rather give more continuity to the data expressed in tables 1, 2, and 3.

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Discussion (Abstract)

Dr. William K. Ishmael, Oklahoma City, Okla. I enjoyed the paper by Drs. Ross and Clardy, I presume because I agree with them. There is little question but that patients with rheumatoid arthritis exhibiting a positive "L. E. prep" have more evidence of generalized systemic disease. It is also important to know the status of the L. E. test in a patient with rheumatoid arthritis, in that it may affect the patient's management. Reactions may result following blood transfusions or the use of various blood fractions. Cold agglutinins may be the cause of untoward reactions.

Our statistics agree with theirs. We have examined 2,840 consecutive admissions to the Arthritis Clinic by means of a "L. E. prep" on patients who had musculoskeletal complaints. Seven hundred and eighty-five, or about one-fourth of this 2,840, were diagnosed as having rheumatoid arthritis. Of the 785, 25 had positive lupus "preps." We used the two-hour clot method, pressing the clot through a screen, then spinning the material down, making a smear of the buffy coat, and staining with Wright's stain.

None of the remaining 2,055 had a positive test for L. E. This group included patients with degenerative arthritis, rheumatic fever, gout, back pain, etc. One significant factor in the group diagnosed as rheumatoid arthritis was that 279 of that 785 had received cortisone prior to their admission. Twenty of this 279 had positive tests for L. E. (7.1 per cent). Twenty of the 25 positive "preps" we have, occurred in patients who had received cortisone therapy prior to examination. Of the remaining 506 patients who had not had cortisone, only five had positive lupus tests (0.9 per cent). This is a ratio of 7.9:1, which may be significant.

I would agree also with Dr. Ross in that one cannot draw conclusions at this time as to the significance of the occurrence of a lupus test in a person with arthritis. I see no reason to call it a false positive. The typical lupus cell either exists or it does not. The pathologist who identifies the cells must use care.

The most important thing, I believe, at this time, is that arthritics with positive lupus cells are inclined to have multiple system involvement. Certainly, these patients do not exhibit all the clinical findings of lupus erythematosus disseminata, and if this is true, then it is doubtful if this test is specific for lupus, but rather is an exhibit of a discrepancy in nucleoprotein metabolism. However, the occurrence of a positive test does warrant caution in the management of these patients.

Dr. Howard L. Holley, Birmingham, Ala. I thought this paper was excellent, and I would like to congratulate Dr. Ross and Dr. Clardy.

It is becoming more and more evident that the L. E. cell phenomenon is not a specific test as was originally thought. We have been interested in this phenomenon in carrying out our research work and its relationship to other diseases. We have seen it in patients in several disease states, most often after allergic reaction. However, we have been most impressed with its occurrences after withdrawal of cortisone or steroid therapy. In fact, we have not seen it in a single patient with rheumatoid arthritis who has not had cortisone.

We have had a patient recently who has been of considerable interest in this regard. This woman was classified as classical rheumatoid arthritis, with repeated negative L. E. cell test, and negative urine and normal white count, and was treated with cortisone which was suddenly withdrawn for an unknown cause. The patient developed a febrile course, a low white count, repeated positive L. E. cell tests, and urinary findings that were consistent with L. E. cells. She is still alive but is being maintained on steroid therapy. The problem arises, did she have lupus erythematosus disseminatus all the time, or did it occur after therapy with cortisone? Certainly she has conclusive evidence for it at the present time.

I believe the crux of the situation is to be found in the fact that our criteria for the diagnosis of lupus erythematosus prior to this time had not been very adequate. We are now coming to realize that lupus erythematosus may be an extremely chronic disease, without evidence of renal damage and with a negative L. E. phenomenon.

As this disease progresses, small blood vessel involvement occurs and the classical findings of disseminated lupus appear. It is interesting to speculate on the relationship of the adrenal steroid and adrenal-cortical function to the pathologic aspects of this disease because it is still controversial as to whether there is any change in the function of the adrenal cortex or not. I think it is fairly reasonable to assume that the adrenal-cortical steroids do offer a protective effect, but whether their sudden withdrawal from a patient with a related disease precipitates the classical picture of lupus erythematosus remains to be seen.

Dr. L. W. Diggs, Memphis, Tenn. Dr. Gouldin and I ("'L.E.' and 'L.E.-Like' Cells," pp. 560-566) consider that the presence of large numbers of neutrophils with velvety and smooth cytoplasmic inclusions of nuclear material is diagnostic of systemic lupus erythematosus, but that similar cells in small numbers may be found in conditions other than lupus erythematosus, and particularly in patients with rheumatoid arthritis. Instead of reporting a given smear as "positive for L. E. cells" one should report "cytoplasmic inclusions of the type seen in lupus erythematosus found in one per cent of the neutrophils." The number of L. E.-like cells should also be reported.

It is always unfortunate when a given morphologic object is given the name of a disease rather than a descriptive terminology, for it forces the examiner to make a clinical diagnosis on the basis of evidence which is often equivocal. Just as the "P. A. poly" is not specific for pernicious anemia, and the "virus lymphocyte" is not specific for viral disease, so the "L. E. cell" is not specific for lupus erythematosus.

The use of the word "tart cell" is also unfortunate for it is neither descriptive nor meaningful. The word "tart" does not have anything to do with resemblance to a cookie with a fruit or jelly inside. "Tart cells" do not have a sharp or sour taste, nor are they female cells of ill repute. The cells were called "tart cells" because they resembled the phagocytic leukocytes observed in the blood smears of a Mr. Tart who was a patient in the Mayo Clinic. It is obvious that the words "tart-like" and "tartoid" are ridiculous.

Dr. Ross (Closing). I want to thank Dr. Ishmael, Dr. Holley and Dr. Diggs for their very kind discussions.

I thank Dr. Ishmael for emphasizing the practical significance of this phenomenon (referred to in the text as a positive L. E. test), whatever its name be. The changes after cortisone withdrawal are particularly interesting. We have seen, as Dr. Ishmael has reported, some patients who have presented the features of a rheumatoid arthritis, who have never been on steroid therapy, and who have had positive L. E. tests. We must admit that most of the patients have been on steroid therapy but most of them have been treated by several physicians before we see them.

As to the nonspecificity of this phenomenon, we do not know what it is specific of, but feel that it probably is specific of some reaction that goes on *in vivo*. In our series of cases, it seemed to correlate very highly with multisystem disease, and these are the only conclusions that we wish to draw from this.

What the Southern means to me—

"The Southern Medical Association was my first love in organized medicine. It came into being the year I entered practice—1906. There were then three sections . . . general medicine, general surgery, and EENT. All were well attended and interest ran high. In response to the needs of men working in special fields, other sections were later added. Expansion has been commensurate with medical progress. The Southern Medical Association has kept pace with the best scientific minds of our nation. . . . We now have twenty specialty sections. Our Journal is second to none; it is the official organ of the Association. Old friends meet, new friends are made, good fellowship abounds, which makes the annual meeting a benediction to all who attend."

—R. L. SANDERS, M.D., *Memphis, Tennessee*

L. E. and L. E. - Like Cells:

A Morphological Study*

E. N. GOULDIN, M.D., and L. W. DIGGS, M.D.,† *Memphis, Tenn.*

The L.E. cell has assumed a prominent place in the diagnosis of disseminated lupus erythematosus since its first description in 1948. The authors describe cells which may simulate the L.E. cell but which they feel are different and may not have the same connotation. In any event this is a laboratory procedure which should play no more than a part in the clinical diagnosis of disseminated lupus.

In 1948, Hargraves, Richmond and Morton[1] reported that they had frequently observed segmented neutrophils containing homogeneous cytoplasmic inclusions of nuclear origin in heparinized bone marrow preparations from patients with systemic lupus erythematosus (hereafter designated as S.L.E.). They introduced the term "L.E." cell. This discovery afforded for the first time, since the original description of the disease by Kaposi,[2] in 1872, a laboratory test with some degree of reliability for the disease S.L.E. The factor responsible for the L.E. cell has been shown to be an antigenically specific gamma globulin[3,4] present in the plasma of the patients with S.L.E. The etiology of this abnormal gamma globulin and the mechanism through which it acts on the nuclei of cells are as yet unknown.

The cytoplasmic inclusion of the L.E. cell has been shown to contain desoxyribose nucleic acid (hereinafter designated as DNA) in a depolymerized state.[5] It is identical optically and chemically to the hematoxylin body[5] and to the fibrinoid material[6] in the connective tissue of the patients with the disease.

It is the purpose of this paper to describe and illustrate the morphologic changes occurring in the nucleus during the formation of the L.E. cell, the morphologic features of the L.E. cell and L.E.-like cells and to present the data obtained from a morphologic study of L.E. preparations from patients with S.L.E. and from non-L.E. patients.

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†From the Department of Medical Laboratories and the Department of Medicine, University of Tennessee College of Medicine, City of Memphis Hospitals, Memphis, Tenn.

The L.E. Cell

The L.E. cell, by definition, is a segmented neutrophil, eosinophil or monocyte, which has phagocytized a nuclear mass "in which the chromatin has lost its structural pattern, has become smoothed out and has taken on a homogeneous appearance."[7]

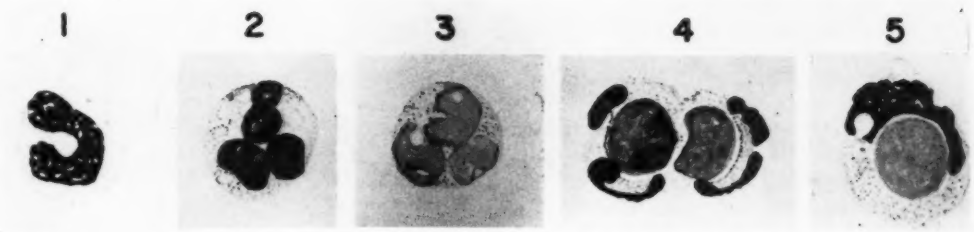
In order for this phenomenon to occur, the following conditions must be met: (1) the *L.E. factor* must be present in an active state; (2) *nuclei* must be present on which the L.E. factor is to act; (3) *cells* capable of phagocytosis of the altered nucleus must be present; and (4) there must be *sufficient time* for the nuclear alteration and phagocytosis to occur.[8]

Morphologically, the alteration in the nucleus during the formation of the L.E. cell is one of nucleolysis which is seen to continue throughout all stages in the formation of the L.E. cell and probably continues even after phagocytosis has occurred.

The authors studied these morphologic changes in the nucleus by taking serial samples every fifteen minutes, for a two-hour period, from a peripheral blood L.E. preparation in a patient with S.L.E. and by making smears of the buffy coat from each sample. The blood was defibrinated with the use of glass beads and the preparation was kept at room temperature. The smears were stained with Wright's stain. The changes observed, which agree with the observations of other workers,[5,9,10] can be divided into three stages as follows:

1. *Stage of Pyknosis.* One or more nuclear lobes undergo condensation with partial or complete loss of chromatin detail. The

FIG. 1



Shows the sequence of morphologic nuclear alterations in neutrophils in the formation of the L.E. cell from serial smears of the buffy coat from L.E. preparation of a patient with S.L.E., Wright's stain. The nuclear alteration is of the symmetrical type with a homogenous appearance and the end product is the typical L.E. cell. 1. Intact neutrophil; 2. Pyknosis; 3. Nuclear swelling with less intense staining of the nucleus; 4. Phagocytosis; 5. L.E. cell.

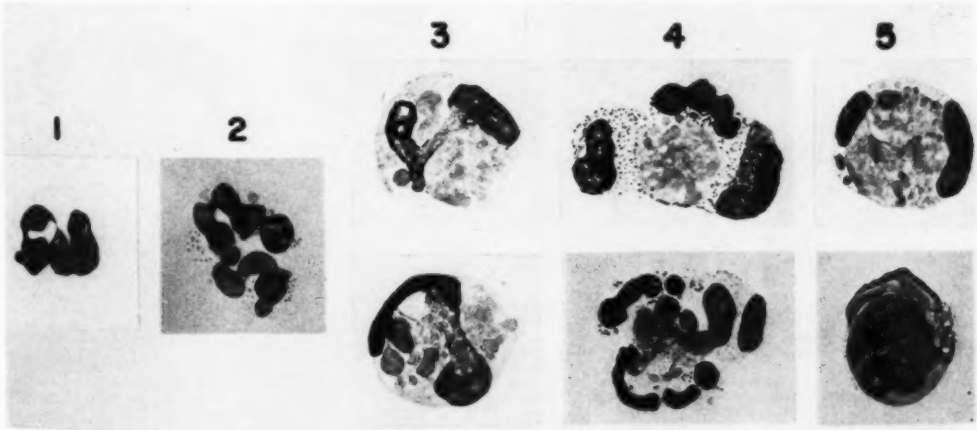
lobes then take a more basophilic stain. (Figs. 1, 2.)

2. *Stage of Nuclear Swelling.* One or more lobes begin to swell, stain less intensely, lose their interlobar filaments and take on a velvety, homogeneous or amorphous appearance. The cytoplasm becomes vacuolated. As swelling of the lobes progresses, it may be accompanied by disruption of the cytoplasmic membrane with separation of the lobes as free masses, carrying with them varying amounts of cytoplasmic fragments (Figs. 1 [3]; 3 [1, 3, 4, 5, 7]).

3. *Stage of Phagocytosis.* The intact cell or lobes of the disrupted cell may be attacked by one or several segmented neutrophils forming in some cases, clumps or rosettes (Figs. 2 [4, 5]; 3 [6]). One or more of these cells may phagocytize a single lobe or multiple lobes and form the L.E. cell (Figs. 1 [5]; 4). The L. E. cell may, therefore, be a single cell with one phagocytized lobe, a single cell with two or more phagocytized lobes, a combination of several fused cells with a single phagocytized lobe, or a combination with multiple phagocytized lobes.

During this study it became evident to us that the nuclear alteration in different cells did not fit into a single pattern. Many variations were observed, some of which are illustrated in figure 3. It appeared to us that the cells belonged to different sequences in the formation of the L.E. cell. We have arbitrari-

FIG. 2



Shows the sequence of morphologic alterations in neutrophils in serial smears of the buffy coat from L.E. preparation of a patient with S.L.E., Wright's stain. The nuclear alteration is of the asymmetrical type with a flaky or lumpy appearance to the nuclear mass. 1. Segmented neutrophil; 2. Beginning nuclear alteration and disintegration of the cytoplasm; 3. Nuclear changes involving the central portions to a greater degree than the peripheral lobes; 4. Rosette formation around flaky and lumpy nuclear mass; 5. Phagocytosis of the altered nuclear material. The lumpy character of the nuclear alteration is more marked in the lower series of cells 3, 4 and 5 than in the upper series.

ly chosen two sequences to classify each cell as follows:

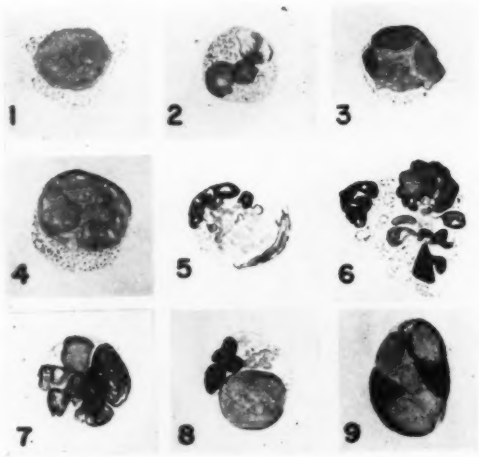
1. Those cells in which the nuclear alteration is symmetrical and generalized, involving all of the lobes alike. The end product here is felt to be the classical L.E. cell with the velvety, homogeneous or amorphous appearance to the inclusion. This sequence is illustrated in figure 1.

2. Those cells in which the nuclear alteration is asymmetrical or focal, involving different lobes or different portions of the same lobe in different degrees. The end product is felt to be a cell with either a flaky or a lumpy inclusion. This sequence is illustrated in figure 2. The cells formed in this sequence are morphologically indistinguishable from some of the L.E.-like cells and are therefore identified in any given preparation as an L.E.-like cell. Whether or not these inclusions later become homogenous and identical to the classical L.E. cell has not been observed.

L.E.-Like Cells

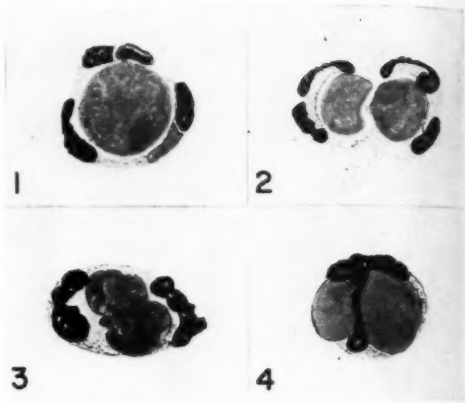
L.E.-like cells, by definition, are cells which morphologically resemble the L.E. cell. (Figs. 5, 6). The term is used here to include all cells having cytoplasmic inclusions of nuclear origin which lack the homogeneous appearance of the classical L.E. cell. Hargraves, Richmond and Morton[1] in their original report on the L.E. cell called these "tart" cells, to be distinguished from the L.E. cell.

FIG. 3



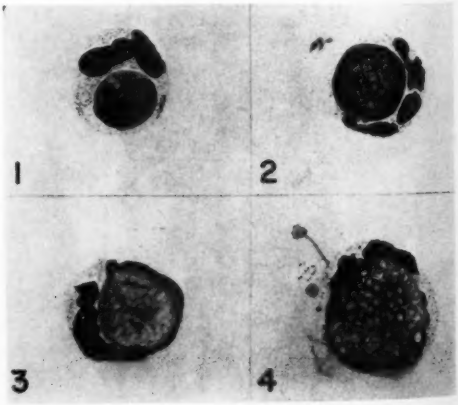
Drawings of random cells encountered in the study of the L.E. formation. 1. Swollen, round nucleus with a fairly homogenous appearance and beginning cytoplasmic disintegration; 2. Early nuclear alteration in nuclear structure with nuclear swelling and fusion of lobes; 4. Changes in structure of nuclear chromatin with indistinct chromatin markings; 5. Variation in degree and appearance of nuclear structure in different portions of the nucleus; 6. Intact neutrophil (left) adjacent to disintegrating neutrophil containing lumpy nuclear chromatin masses; 7. Swollen and clover-leaf nucleus with varied types of nuclear alteration; 8. L.E. cell containing with its cytoplasm a nuclear inclusion having minimal residual chromatin structure; 9. L.E. cell containing multiple lobar and fairly homogeneous structures. In cells 8 and 9 the nucleus of the phagocytizing cells is likewise undergoing alterations.

FIG. 4



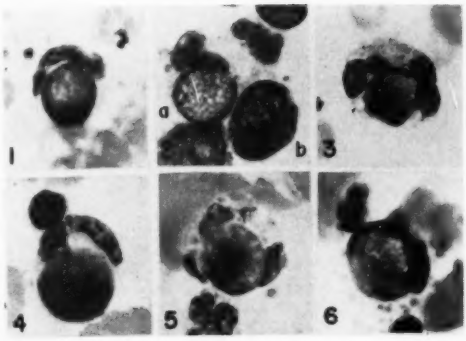
Drawings to show variants of the L.E. cell. 1. L.E. cell which appears to have been formed as a result of three segmented neutrophils phagocytizing one nuclear mass and then fused to form one cell; 2. Two segmented neutrophils containing within their cytoplasm two nuclear inclusions; 3. Two segmented neutrophils with fused cytoplasm containing within their cytoplasm a double-lobed nuclear mass; 4. A segmented neutrophil with two cytoplasmic inclusions having relatively smooth and homogeneous appearance.

FIG. 5



Drawings of L.E.-like cells to illustrate the types commonly encountered. Each cell is a segmented neutrophil which has phagocytized a nuclear mass. 1. The cytoplasmic inclusion has visible chromatin structure and focal condensation; 2. The chromatin structure is linear and plainly visible; 3. The inclusion has lost much of its chromatin structure and has taken on a flaky or fluffy appearance and a dark rim; 4. The inclusion is quite large with visible chromatin structure having a coarsely granular appearance.

FIG. 6



Photomicrographs of L.E.-like cells from six of the eight patients studied (Table 2). 1. Neutrophil with an inclusion which shows some nuclear alteration but still retains some visible structure (Case 1); 2. Neutrophil (a) and monocyte (b) having inclusions with visible chromatin structure (Case 2); 3. Neutrophil with inclusion having poorly defined chromatin markings (Case 3); 4. Neutrophil with relatively smooth and homogeneous inclusion body having minimal visible chromatin structure (Case 4). This cell is indistinguishable from the L.E. cell; 5. One or possibly two neutrophils with inclusion having visible chromatin structure, but showing some nuclear alteration (Case 5); 6. Neutrophil with inclusion having a lumpy appearance (Case 8).

Morphologically the cytoplasmic inclusions of the L.E.-like cells have one or more of the following characteristics: (1) visible chromatin structures; (2) flaky, coarsely granular, or lumpy appearance; (3) one or more dense, dark-staining nuclear masses without visible chromatin strands; and (4) a dark-staining margin.

The L.E.-like cells most commonly encountered are illustrated in figure 5. These cells can be distinguished readily from the L.E. cells. On occasions one will encounter L.E.-like cells which are difficult to differentiate morphologically from the L.E. cell, even by the most expert observers.[7] The cells that incite this difficulty are usually ones which contain an inclusion with a fine, flaky appearance. On rare occasions one encounters cells morphologically indistinguishable from the classical L.E. cell in conditions other than S.L.E. (Case 4, Table 2; Fig. 6 [4]). Notable examples of the latter are seen in cases of hypersensitivity to penicillin[11-13] and toxic reactions to hydralazine hydrochloride.[11-18]

S.L.E. and Non-S.L.E. Case Study

With the morphologic features of both the L.E. and L.E.-like cells in mind, 13 cases of S.L.E. (Table 1), 8 of which were proved by autopsy, were studied. In like manner, 8 cases

TABLE 1

NUMBER OF L.E., L.E.-LIKE CELLS AND ROSETTES IN L.E. PREPARATION OF BLOOD FROM PATIENTS WITH S.L.E.

Case No.	No. per 1000 Neutrophils L.E. Cells	L.E.-Like Cells	Rosettes
1.*	134	12	7
2.	112	26	26
3.	103	13	28
4.*	92	25	27
5.*	92	23	61
6.	82	64	75
7.*	78	28	16
8.*	44	10	2
9.	34	3	2
10.*	19	12	5
11.*	12	16	5
12.	6	52	24
13.	6	12	1

*Confirmed by autopsy

of non-S.L.E. (Table 2), in which L.E.-like cells were found, were studied by the authors. The preparations in both series were from bone marrows in some cases and from peripheral blood in others. No distinction is made as to the L.E. preparation technic used. A total of 1,000 neutrophils were counted and in each case the number of L.E. cells, L.E.-like cells and rosettes were recorded. The L.E. cells recorded were of the classical type, in which the inclusion had a homogeneous appearance with no visible chromatin structure. A sharp line of differentiation between the L.E. cell and the L.E.-like cell was not always evident as might be indicated in the tables. All types of L.E.-like cells were observed in each case. It was arbitrary whether to call some of the cells encountered L.E. or L.E.-like cells. Fortunately, these borderline cells were few in most instances.

The results of the study on the cases of

TABLE 2

NUMBER OF L.E., L.E.-LIKE CELLS AND ROSETTES IN L.E. PREPARATION OF BLOOD FROM PATIENTS WITH NON-S.L.E. CONDITIONS

Case No.	No. per 1000 Neutrophils L.E. Cells	L.E.-Like Cells	Rosettes	Diagnosis
1.		15	8	Undetermined
2.		30		Acute Rheumatic Fever
3.		24	16	Rheumatoid Arthritis
4.	3	7	4	Rheumatoid Arthritis
5.		6	1	Undetermined
6.		6		Post Hepatitis Cirrhosis
7.		6		Undetermined
8.		16		Tuberculosis

S.L.E. are listed in table 1. The following observations are made from this data: (1) the number of L.E. cells, L.E.-like cells and rosettes are very variable in different cases; (2) the number of L.E. cells are quite high in some cases, over 10 per cent in three and over 5 per cent in seven; (3) the number of L.E.-like cells are relatively high; (4) there is no definite correlation between the number of L.E. cells, L.E.-like cells and rosettes.

The results of the study on non-S.L.E. cases in which L.E.-like cells were seen are listed in table 2. The following observations are made from this data: (1) the number of L.E.-like cells are quite variable in different cases; (2) rosettes are present in half of the cases; (3) one case had cells morphologically indistinguishable from the L.E. cell. This case was a 60 year old white woman, who had a history of rheumatoid arthritis of 14 years duration, characterized by deformed, ankylosed joints, rheumatoid nodules and there was no evidence of renal involvement.

Discussion

There are students[13, 19-23] of the disease who feel that S.L.E. is an auto-immune disease. In support of this concept is the work of Rich,[19] who produced vascular lesions, identical to those seen in S.L.E., in experimental animals by anaphylactoid reactions to foreign protein. Furthermore, patients with the disease frequently have histories of allergies. Reactions to drugs and blood transfusions, hemolytic anemia and thrombocytopenic purpura frequently accompany the disease. An acute exacerbation is not infrequently preceded by an allergic reaction.

In further support of this concept is the similarity of the L.E. factor to an antibody. It is a specific gamma globulin[3,4] that is inactivated by bacterial action and on heating to 65 degrees[24,25] and it is active at room temperature for several months.[5,24,25]

Recent work[6] on the histochemistry of the hematoxylin body and fibrinoid material has shown that it is the DNA of the nucleic acid component of nucleoprotein that undergoes depolymerization, degradation and eventful disappearance. It has also been shown that the hematoxylin body is identical optically and chemically[5] to the L.E. cell. Since the L.E. factor is necessary for the formation of the L.E. cell, it follows that it is probably the L.E. factor that is responsible for the degradation of nucleic acid which gives rise to the hematoxylin body, fibrinoid material and the L.E. cell. The question that follows is whether or not the L.E. factor is produced as a result of the body becoming sensitized to the DNA. Further work on this subject is needed.

From the above facts a theory for the pathogenesis of the disease is proposed:

Autosensitization to Unknown Antigen (? DNA)
Gives rise to:
L.E. factor (a specific gamma globulin, ? antibody)
Which acts on:
Nucleic acid component of nucleoprotein
Producing the:
1. *L.E. cell*
2. *Hematoxylin body*
3. *Fibrinoid material*

A positive L.E. test has been reported in a number of diseases other than S.L.E. However, when the cells in the photographs of these reports are put under critical appraisal, from a morphologic standpoint, most of the cases fall short of the criteria for the L.E. cell. Many of these cells would now be classified as L.E.-like cells. There remain however, some cases in which the cells fulfill the criteria for the L.E. cell. These cases, for the most part, have been reported in hypersensitivity reactions to penicillin and in toxic reactions to hydralazine hydrochloride.

This brings us to the question as to how a L.E. test should be reported. It is customary for many laboratories to report the L.E. test as positive or negative. When it is reported positive, no distinction is made between L.E. and L.E.-like cells or the number of each. Positive reports would, therefore, have different meanings in different laboratories.

Whenever L.E. or L.E.-like cells are seen, it is recommended that 300 to 500 segmented or band forms of neutrophils be counted and the number of L.E. and L.E.-like cells per 100 neutrophils should be recorded. If no L.E. or L.E.-like cells are seen in the 300 to 500 neutrophils counted, but some are seen on searching, it should be reported as such. If on searching, no L.E. or L.E.-like cells are seen, it should be reported as follows: "No L.E. or L.E.-like cells are seen on searching."

The reliability of the test is directly dependent upon: (1) the accuracy instituted in carrying out the procedure; (2) the ability of the observer to differentiate the L.E. cells from the L.E.-like cells; and (3) the number of L.E. cells present in the preparation. The results of this test in the hands of inexperienced observers would not be as reliable as the results obtained by such men as Hargraves and Haserick. When classical L.E. cells are present in large numbers, over 1 per cent for example, the test carries with it a high degree of reliability. L.E. cells have been reported in 70 to 100 per cent of cases of S.L.E.

In speaking of the specificity of the L.E. cell and the L.E. test, the authors raise the following questions: Do the L.E. cells in conditions other than S.L.E. have the same histochemical alteration to the inclusion as the L.E. cell? Do conditions other than S.L.E., in which classical L.E. cells are found, have an abnormal gamma globulin identical to the L.E. factor? Is S.L.E. a specific disease with a specific etiologic factor or is it a syndrome with more than one cause? With the present limited knowledge of the disease, the authors prefer to use the term reliability when speaking of the L.E. cell and the L.E. test and to hold the term specificity for further work on the subject. It is hoped that, by avoiding the term specificity, some of the confusion in the minds of physicians receiving the report of the test will be prevented.

It should be remembered that the L.E. test is a laboratory procedure and as such has certain inherent errors. It is, therefore, important that the results of the laboratory test be interpreted in light of the clinical picture to arrive at the diagnosis of the disease S.L.E.

Summary and Conclusions

Smears of the buffy coat of defibrinated blood of patients with systemic lupus erythematosus were made at 15 minute intervals after collection. The first change observed was a pyknosis of the nucleus. This was followed by a swelling of the nucleus, a disappearance of interlobar filaments and a loss of distinct chromatin markings. In the majority of cells the nuclear alteration was symmetrical, producing lobes having a smooth or homogeneous appearance. In other cells the nuclear alterations were asymmetrical, often involving one portion of the nucleus more than others and producing a flaky or lumpy nuclear appearance. In association with the more advanced nuclear changes the cytoplasm distintegrated. The mass of altered nuclear material was phagocytized, usually by other neutrophils. The phagocytosis of the smooth and homogeneous nuclear masses produced the classical L.E. inclusions as described by Hargraves and associates, whereas the phagocytosis of the flocculent or lumpy masses led to the production of L.E.-like inclusions which cannot be distinguished from those seen in numerous non-S.L.E. conditions.

L.E.-like cells differ from typical L.E. cells in that the inclusions are not smooth and homogeneous, but are unevenly stained and have residual chromatin structures. L.E.-like cells frequently have prominent and dark margins, whereas typical L.E. cells have little or no peripheral condensation of chromatin.

The number of L.E. cells, L.E.-like cells and rosettes in relation to the neutrophils in L.E. preparations from 13 patients with S.L.E. varied from 0.6 L.E. cells per 100 neutrophils to 13.4 per 100. There was poor correlation between the number of typical L.E. cells, L.E.-like cells and the number of rosettes. In smears of buffy coat of blood from eight patients with conditions other than S.L.E. who had demonstrable L.E.-like cells, rosettes were demonstrable in four. Cells indistinguishable from the typical L.E. cells were demonstrated in one patient with rheumatoid arthritis.

The so-called L.E. cells are not specific for S.L.E. The reliability of the diagnosis is increased in proportion to the number of typical L.E. cells seen. The diagnosis should be made on the basis of combined laboratory and clinical findings and not on the basis of morphology alone.

It is recommended that the reports of the L.E. preparations state the number of L.E. and L.E.-like cells per 100 neutrophilic leukocytes, based upon the examination of 300 or more leukocytes.

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Discussion (Abstract)

Dr. H. R. Pratt-Thomas, Charleston, S. C. This paper has been music to my ears, and I think the authors are to be congratulated.

I believe it has become generally accepted, particularly by internists, that the L.E. cell is a specific diagnostic feature of disseminated lupus erythematosus. On the other hand, the morphologic picture of disseminated lupus erythematosus, at least in so far as we are concerned, has been covered by considerable confusion. This has progressed to the extent that if an L.E. cell is present in a preparation prior to death and then if at autopsy we are unable to find any morphologic changes substantiating the diagnosis of L.E., we have been accused, as pathologists, of not knowing what we are looking for or of not being able to see it, which, to some extent, I resent.

I think the question arises as to the specificity of this change and whether or not it is always possible to differentiate the L.E. cell from the L.E.-like cell. One wonders whether or not a lot of these cases in which assiduous attempts to make the morphologic diagnosis of lupus erythematosus have failed that we have been trying to do it on the basis of L.E.-like cells. The problem of L.E. cells has practically revolutionized my thinking as to what lupus erythematosus really is. Can you diagnose it on the basis of L.E. cell alone, is it a morphologic, anatomic entity which is specific, or is it something in the realm of chemistry alone which may not leave any morphologic trace within the body?

I think this has been an extremely interesting and well-illustrated talk which I have enjoyed and appreciate very much, and I certainly hope that further work is continued in this direction.

50th Anniversary Meeting

Washington, D. C.

November 12-15, 1956

Cancer Charlatanism

CHARLES E. HORTON, M.D.,† HUGH H. CRAWFORD, M.D., CARTER P. MAGUIRE, M.D., NICHOLAS G. GEORGIADE, M.D., and KENNETH L. PICKRELL, M.D.,* *Durham, N. C.*

The problem of cancer quackery may be as great if not greater than at any time in the past, because of an aging population and therefore an increasing incidence of basal and squamous cell carcinomas. This paper points up a situation in which the medical profession should take a hand.

OF THE MANY TRAGEDIES which physicians encounter, none is more disheartening than to be consulted by a patient with an extensive or an incurable carcinoma who has been treated by a quack cancer healer with a "secret" remedy. Although we may think of cancer charlatans as prospering only in an era of the past, this, unfortunately, is not true. Even today it is estimated that thousands of patients are currently being treated by quack healers. While it is true that charlatanism flourishes primarily among the uninformed, it is not uncommon for a healer who possesses a pleasing or a persuasive personality to develop a large and devoted following in many classes of society.[1]

Since a common cause of neoplastic disease remains obscure, the cancer quack exploits this fact and, in addition, emphasizes that even physicians admit that they cannot cure all cancers. At the same time, they offer hope to the patient by stating that they have a secret sure cancer cure without operation, which medical science does not possess.[2,3] Others claim to hold an ancient remedy of the Egyptians which has only recently been rediscovered. Only a few charlatans profess to have undertaken scientific study resulting in the secret discovery of both the cause and the cure for cancer.[4]

Historical Review of the Treatment of Cancer

The ancients recognized cancer as a disease, for it is mentioned in the Ebers Papyrus (B.C. 1500) and in the oldest literature of India and Persia. The early Egyptians treated cancer by excision and with a variety of escharotic pastes, including a form of arsenic ointment which many charlatans use at the present time. Hippocrates (B.C. 460-375) burned out a tumor of the neck, the first recorded use of the actual cautery. Celsus (B.C. 30-A.D. 138) excised a breast cancer, while Cato and Pliny used charcoal and a variety of internal medications to draw out the disease. Leonides of Alexandria (A.D. 180) removed an extensive breast cancer, using both the scalpel and cautery, and approached closely the concept of the present-day operation. From that time to about 1700,[6] little progress was made in the treatment of cancer. This may have been due, in part, to the ban of the Church upon the performance of surgical procedures.

It is of interest to learn that in 1758, after debating whether or not to rebuild the Capitol which had burned a short time previously, our first President, Mr. Washington, together with Mr. Blair, Mr. Madison, and the delegates to the House of Burgesses at Williamsburg, Virginia, voted a 100 pound reward for "a receipt of curing cancers." The recipient of this award was a Mrs. Johnson who made her remedy of garden sorrel, celandine, persimmon bark, and spring water. But in spite of this "receipt," the colonists apparently were still afflicted with cancer. Dr. Benjamin Rush, a signer of the Declaration of Independence, preferred his own cancer remedy which consisted of Fowlers solution, zinc oxide, and garlic juice.[5]

We have collected, from many sources,[7-9] a list of 62 "cures" which have been used as cancer remedies since 1700[10,11] (Table 1).

Cancer Quackery at the Present Time

We have had an opportunity to see and study 64 patients who allegedly have had cancer and who were treated by cancer quacks. At the present time we know of seven practicing cancer charlatans in North Carolina and Virginia. On one occasion we were permitted to visit the home "office" of one of

†New address, 611 Medical Arts Building, Norfolk, Va.

*From the Division of Plastic and Oral Surgery, Duke University School of Medicine and Duke Hospital, Durham, N. C.

these healers to watch the treatment, and to obtain some of the ointment for analysis. On another occasion, the cancer charlatan himself sought our advice and treatment for a large squamous cell carcinoma of the forehead which he did not want to treat with his own remedy! This patient became very grateful and later offered his "knowledge" and "remedies" for our study. Since cancer quacks are notoriously secretive about their treatments, this information stimulated our interest in the subject of quack cancer cures, resulting in the present report.

It is of interest to report the maneuvers and folklore involved in the preparation of some escharotic pastes which we have investigated.

TABLE 1

CANCER QUACK CURES

1. (1767) Dr. J. Burrows advocated the use of milk of goats fed on hemlock for cancer.
2. (1817) Ashby claimed cancer was due to worms, and manufactured a specific anti-worm medicine. He was exposed as a faker when caught sliding "cancer worms" out of his sleeve into a lesion.
3. (1780) Justamand used an escharotic paste of antimony, arsenic, and egg white for cancer.
4. (1856) Velpeau used sulphuric acid and saffron as cancer paste.
5. (1857) Dr. Fell used bloodroot, zinc chloride, flour and cochineal for carcinomas.
6. (1857) The Vienna paste of potash and quicklime was used for carcinomas.
7. (circa 1857) Arsenous acid, cinnabar and burnt sponge were used by Maneck for cancer.
8. (circa 1857) Conquoin advocated cancer treatment with zinc chloride and flour as cancer paste.
9. During this period, Bourgard used arsenic, cinnabar, corrosive sublimate, zinc chloride, sal ammoniac, flour and starch in a cancer paste.
10. In 1850, Marsden experimented with arsenous acid and muscilage of gum acacia for cancer therapy.
11. Also in 1850, Michel used sulphuric acid and powdered asbestos as a cancer cure.
12. In America, circa 1875, a Mrs. Joe Person of North Carolina used an Indian medicine remedy of unknown herbs and whiskey. Possibly this is a portion of the formula which was given to us 80 years later.
13. Baking soda
14. Saltpeter
15. "Synthetic anti-toxin"
16. Distilled water
17. Calcium free diet
18. Rhododendron paste
19. Vinegar
20. Red clover leaf poultice
21. Red clover tea
22. Chloride of zinc, bloodroot, and wheat flour
23. Fig leaves
24. Arsenic
25. Zinc
26. Lead
27. Mercury
28. Bloodroot
29. Bluestone
30. Sorrel
31. Plantain leaf
32. Croton oil
33. Pokeweed
34. Potato poultice
35. Cottonseed oil
36. Alcohol and water
37. Tannin and carbolic acid
38. Resin and beeswax and fat
39. Acetic acid
40. Potassium iodide
41. Sodium sulfide and limburger cheese with glycerine
42. Quinine sulphate
43. Zinc and burnt peat
44. Germex
45. Grafonol (sand and calcium oxide)
46. A diet of carrot juice with milk
47. Hoxin
48. Alum injections
49. Cod liver oil
50. Sarsaparilla bark
51. Hemlock
52. Potash
53. Iodine
54. Bromine
55. Camphor
56. Morphine
57. Gold
58. Antimony
59. Sourinol (mineral oil with cinchona and ichthyol)
60. Trioray (cure of cancer by colored lights)
61. Bio-Dynomio-Chromatic (cure of cancer by colored lights)
62. Spectrochrome (cure of cancer by colored lights)

In the first preparation, two salves were employed for the "complete cure." The first salve was called the "killin' salve;" the second was the "drawin' salve." To prepare the first salve: "After gathering sheep sorrel from the woods, the herb is placed in a rag and beaten thoroughly. Squeeze the juice into a round pewter basin and set in the hot sun until a thick green paste is formed. Next, place sweet gum bark in a wool sock and boil to produce a black paste. Mix equal parts of the sorrel paste and the sweet gum bark paste to produce a greenish-black salve—the 'killin' salve.' The 'drawin' salve' is prepared by boiling chestnut oak bark to a white paste, then mix with equal parts of mutton tallow, pine resin, and coon root."

To cure a cancer, "place a small amount of the 'killin' salve' on the lesion. Around this, place a dam of flour paste to aid in localizing the 'killin' paste.' Tape this in position for 48 hours. During this time, the pain may be extreme. After 48 hours, remove this ointment and tape in place a similar amount of the 'drawin' salve.' Remove this in 48 hours and a 'plug of tissue will let loose'—this is the cancer. If streaks remain in the base of the raw area, this is indicative of persistent cancer roots and more 'killin' paste' is needed. Generally, three times will cure any cancer." When asked about the resulting scar, the quack was quick to say, "The scar ain't bad—it generally heals in 6 to 8 weeks and it's better than dying of cancer, ain't it?"

Another remedy investigated was used widely for "small" cancers. This was prepared by mixing the white of two eggs, two teaspoonsful of salt, one tablespoonful of bee honey, and a teaspoonful of bluestone dust. Place this in equal parts of warm water and homemade apple vinegar. "Apply as a paste for 48 hours for small cancers, whether they are malignant or not," was the sage advice given in using this salve.

We have been impressed however, with the genuine basic honesty of a few of the quack backwoods healers. It is our opinion that some of these people are true believers in their remedies, and that lack of education, not the desire for exploitation of the masses, is the real cause of this evil. In other cases this is not so, for now practicing in Texas is a "cancer healer" named Hoxsey, who is a 52 year old naturopath with an eighth grade education.

By his own admission, he has been arrested more than 100 times in the past 30 years, and even though the American Cancer Society, the American Medical Association, and the U. S. Food and Drug Administration have denounced him as a fraud and branded his concoctions as worthless, he is now reported to see more than 40 new patients each day.[12]

Occasionally, senators are susceptible to the lure of quack healers. Pennsylvania State Senator John Haluska was reported to be one of Hoxsey's ardent admirers. After his 35 year old sister took Hoxsey's cancer cure, she told him, "I don't care whether it's cough syrup or pure mountain water, that's what I owe my life to."[13] United States Senator Tobey of New Hampshire was a strong advocate of a quack cancer healer in New England, who allegedly cured his son of cancer, although this cure was never substantiated scientifically. Senator Tobey even intimated that physicians were not doing all in their power to treat cancer, perhaps because doctors were afraid they would lose patients and money if cancer were cured.[14,15] Even Senator Langer was criticized strongly in an article in the *Journal of the American Medical Association,* in 1948, for the abuse of his franking privilege for the circulation of propaganda for Koch's cancer quackery.[16]

More recently, in 1954, Kenneth Crook, from Lone Rock, Wisconsin, turned away hundreds of "customers" because of lack of room in his "tunnel" which was "packed" with low grade uranium ore in cushions. Crook was paid one dollar an hour by persons who sat in the enclosure in hopes of curing cancer and other ailments. A state official who measured the ore in the tunnel with a Gieger counter described its radioactivity as about equal to that of a radium dial wrist watch.[17]

In a magazine called *Dare,* prominently displayed for sale on newsstands throughout the United States in March, 1954, an article was written by an unknown author in which he frankly concludes, "The medical profession seems more interested in retaining its present lucrative methods than in investigating other inexpensive nonsurgical cures for cancer. At least five cures, the Koch, Hoxsey, Lincoln, Coca, and Gerson are proving effective in cancer treatment."[18] It is almost unnecessary to say here that the American Medical Association has branded the above "outright quackery and fraud."

To further confuse the uninformed, a 24 page publication was recently sent to rural mail-box holders in Durham, and presumably to similar cities in the United States, from an institution in Colorado. This pamphlet is covered with professions of former patients treated with a so-called cancer cure of a new internal, external, and dietary method. They state plainly that x-ray, radium, and surgery are harmful and, although they assure the reader that the medical doctor is probably an honest man doing all in his power to treat malignancy, they wish that "regular doctors" would not meddle with cancers, since x-ray, surgery, or radium make the cure more difficult when the terminal patient ultimately comes to Colorado for treatment.

In Wichita, Kansas, a magazine is published monthly called *The Defender,* in which the editor praises without restraint the Lincoln bacteriophage treatment and the Hoxsey system. In this publication are pages of testimony from patients allegedly cured of cancer. Advertising is printed from men in various locations offering to the public the benefit of the Koch, Hoxsey, and Lincoln treatments. Cures are offered in the states of Washington, Arkansas, Kansas, Texas, California, and Georgia. The editor of this journal broadcasted the following message which was printed in the November, 1954, issue of *The Defender:* "And yet there are men, cruel men who, for financial reasons and out of professional jealousy, are trying to keep this information from reaching the public. They throw road-blocks in Dr. Hoxsey's way at every turn. But truth is might and must triumph in the end. Despite opposition, millions of people know tonight that cancer, both internal and external, is being cured at Dallas."

Fortunately, not all publications are so flagrantly critical of the medical profession. Of real service has been the accurate reporting of quackery in *Time, Newsweek,* the Boston newspapers, and many other reputable publications which attempt to report the truth. However, the continuing damage done by alarmist pulp prints, by uncensored and uncontrolled radio broadcasts, and by the comments of uninformed, even well-meaning people, as to the efficacy of unorthodox cures

FIG. 1

Widespread basal cell carcinoma unsuccessfully treated with cancer paste. Controlled with wide excision and grafting.

FIG. 3

Extensive basal cell carcinoma unsucessfully treated with cancer paste. Note the degree of resection necessary to control the spread of tumor under grossly normal appearing skin.

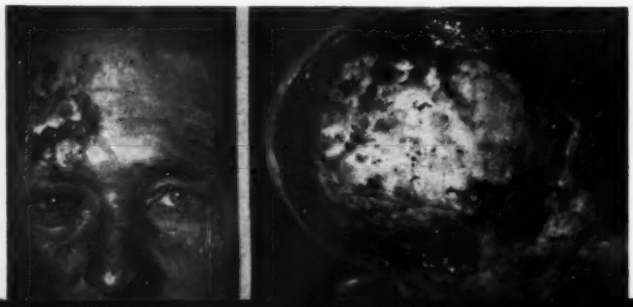

FIG. 4

Widespread squamous cell carcinoma of nose and cheek in 72 year old male. Controlled with excision of nose, cheek, and maxilla. Rehabilitated with a temporary prosthesis.

FIG. 2

Destruction of nose by cancer paste (lupus erythematosis). Reconstruction with adjacent cheek tissue.

FIG. 5

Destruction of left alar wing by cancer paste. Reconstruction with nasofacial flap.

FIG. 6

Patients who have received cancer quack therapy.

for cancer has now truly reached alarming proportions. The advertising of charlatans is reaching hundreds of thousands of people, who are not being adequately informed by legitimate teaching of the medical profession.

Clinical Material

In view of this modern charlatanism, it is essential to examine the end results of patients who have submitted to cancer quack treatment, in order to have a sound basis for the judgment of such care. In our investigation of this problem, the case histories of 64 patients who had been treated by cancer quacks before seeking help at Duke Hospital were reviewed. It became apparent early in this study that we probably do not see the usual patients who receive quack treatment. It is quite possible that a high percentage of these patients have benign lesions which are destroyed by escharotics, and also it is quite true that a small percentage of early carcinomas may be cured with cancer paste. Therefore, if we assume that the cancer quack has "successful treatments" as well as failures, we must consider the number of patients seen at Duke making up only a small portion of the North Carolina cancer quack clientele, and assume that hundreds and perhaps thousands of satisfied patients of the quack doctors in the country at large are now living and advertising their cures.

An analysis of these 64 available charts reveals several important findings. We have arbitrarily divided the patients into three groups, according to the stage of disease encountered at Duke Hospital following treatment by the cancer quack elsewhere.

(1) The first group consists of those who by history alone probably did not have carcinoma when the cancer healer began treatment. Typical of this is the patient who entered the clinic with her nose totally destroyed by escharotics, yet who proclaimed the wonderful treatment that had cured her cancer. After questioning, the patient described her original lesion as similar to a small hemangioma which was present on the cheek. Ten of the 64 patients examined gave a history which raised grave doubt that a cancer ever existed before treatment by the quack. However, three of the patients had an almost total destruction of their noses by the cancer paste, and another had extensive loss of tissue of the cheek. When these areas were biopsied prior to reconstruction of the absent parts, no histologic evidence of carcinoma was found. Three of these patients had senile keratoses elsewhere on their faces which they described as "cancer," three had lupus erythematosis proven by biopsy and histologic section, and the remaining patients had benign nevi.

(2) The second group contained those patients who had been treated by cancer quacks and, after treatment, presented themselves at Duke Hospital with evidence of noncured, persistent cancer as proven by biopsy and histologic study. This group consisted of 27 patients who, in spite of their procrastination and improper treatment, were still theoretically curable by surgery. In this group, we encountered 19 basal cell carcinomas, seven squamous cell carcinomas, and one melanoma. Ten lesions were on the nose, six on the cheek, six on the forehead, two on the hand, two on the neck, and one on the chest.

(3) Most serious, however, was the third group of patients who, because of prolonged quack treatment had incurable malignant lesions when they first sought our advice. Twenty-seven patients in our group of 64 were found to be incurable at examination in our clinic. In this group, we encountered 21 squamous cell carcinomas, five basal cell carcinomas, and one sarcoma. These were located as follows: five lesions were on the lip and oral cavity, five in the nose and accessory sinuses, four on the chin and neck, three on the cheek, four on the forehead, three in the eyelids and orbit, two in the parotid area, and one on the hand.

One of these patients brought the "core" of her cancer which had sloughed after application of the cancer paste, and which she had preserved in alcohol. Microscopic examination disclosed many strands and cords of mitotic cells undergoing necrosis. Needless to say, however, the tumor was not cured and the patient died soon after being seen.

Discussion

It is significant to note that in the patients treated by cancer paste and who still had "active" cancer and were salvaged by surgery, the predominant lesion was the basal cell carcinoma. Conversely, in the patients who had persistent incurable cancer on admission to Duke Hospital, the predominant lesion was of

the squamous cell type, which is characterized by rapid growth and distant metastases.

Another interesting observation in this series was that in the 64 cases studied, there was not a single negro patient, although the percentage of colored patients seen in our clinic is quite high. This may be due in part to the fact that no colored cancer quacks have been found in this area, and that only limited opportunities exist for colored patients to seek quack treatment.

There may be many reasons why patients turn to unorthodox practitioners. In a psychologic study of such victims, Cobb[19] reports that they may be divided roughly into four groups: (1) miracle seekers, those who believe that a miracle might happen to save them the ordeal of surgery; (2) the uninformed, those who do not know the dangers of quackery; (3) the restless, those who do not want deliberation and study regarding their problem, and quacks will see and treat patients immediately; and (4) the graspers at straws, those for whom the doctors have done all they can and yet no cure is available, "for their own peace of mind they must continue to try and do everything possible for as long as they can."

In our series, we have not attempted to evaluate the psychologic motives of patients who consult charlatans. However, it is our firm conviction that ignorance and lack of education is by far the most common cause. Over and over has been heard, "But doctor, he told me he could cure me without surgery."

The great tragedy in this series is the loss of life of the 27 patients who might have been saved had they received proper treatment rather than meddling and bungling by self-appointed cancer healers. Of lesser importance are the 10 patients who are mutilated for life. Most fortunate in this group are those 27 patients who recognized the deficiency of their cancer quack treatments, who sought medical advice, and who are now without evidence of disease (Figs. 1-6).

The deficiencies of cancer quack therapy are obvious. First, no biopsies are taken and any lesion may be treated as a cancer whether it is malignant or not. Second, there is no control as to the adequacy of treatment, the judgment of an untrained, unscientific charlatan is final. Third, caustics may cause widespread and unnecessary loss of normal tissue, which need not have been destroyed had microscopic study of the specimen been employed. Fourth, the scars resulting from escharotic material are always larger and more undesirable than those resulting from surgical excision or radiation, and no attempt at repair of the defect can be accomplished by the charlatan; and fifth, and most important, many quack cures have no effect whatsoever on malignancy and are worthless in the treatment of cancer.

Although most cancer quacks do not make a specific charge for treatments, the patients are told without fail that they can give a donation of any amount they desire to show their appreciation. The usual amount given by our patients was from five to ten dollars per treatment.

As physicians, it is our duty and our obligation to do everything possible to stop this charlatanism which results in unnecessary death, unwarranted mutilation, economic loss, and mental anxiety. In the United States the course to follow is clear. When any physician hears of a practicing charlatan, he should notify his state board of medical examiners, giving the name and address of the particular person, with the request that his activities be investigated to determine whether or not he is violating the medical practice act.

In the case of those charlatans who persistently refuse to stop their undesirable activities, our medical societies must call upon leaders in the legal profession to aid in drafting new laws and new penalties which will be so severe as to certainly deter premeditated quackery. This does not mean the medical profession should repulse in an arrogant manner all well-meaning individuals who propose various anticancer agents. We have a duty to examine and study each new proposal of a cancer cure, no matter how unreasonable it may seem, so that we may never be accused by honest, informed sources of attempting to suppress new and efficient treatment of cancer. However, it is also our duty and responsibility to inform and protect the public from the menace of cancer charlatanism, which in this modern age, even at this present time, is ever increasing.

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GOLDEN ANNIVERSARY CELEBRATION
SOUTHERN MEDICAL ASSOCIATION

The Read House, Chattanooga, Tennessee

October 2-3, 1956

It will be remembered that upon call of Dr. G. C. Savage, then president of the Tennessee State Medical Association, Nashville, in 1906, representatives from Alabama, Florida, Georgia, Louisiana, Mississippi and Tennessee met at The Read House in Chattanooga, October 2-3, 1906, and organized the Southern Medical Association. At later meetings other states were added, making the sixteen states and District of Columbia now comprising the Association. The Council of the Southern Medical Association at the annual meeting in Houston, Texas, November 14-17, 1955, unanimously approved a suggestion that the Association have a Golden Anniversary Celebration at The Read House in Chattanooga, October 2-3, 1956, exactly fifty years from the day the Association was organized. The Council designated Mr. C. P. Loranz to be chairman of the Celebration Committee, the President to appoint the other members of the Committees. Since the Association was organized in Chattanooga, it has held one of its annual meetings there, its sixteenth, November 1922.

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Revised Technic in Perineal Prostatectomy: Report of 110 Cases*

HOMER R. JUSTIS, M.D., and HAMILTON W. McKAY, M.D.,
Charlotte, N. C.

The perineal approach to the prostate has much to recommend it under certain circumstances. The authors describe the advantages of their technic.

THE OBJECT OF THIS PRESENTATION IS TWOFOLD. First, we would like to emphasize certain changes in the technic of simple perineal prostatectomy as compared to the original Young operation. Secondly, we would like to review our results in 110 cases of the operation performed by a modified approach. This essay is not in any sense a discussion of which of the operations is the superior procedure, but is an attempt to demonstrate the merits of the perineal approach and to erase fear of complications which, in our experience, have not occurred with the revised technic. The four standard operations of prostatectomy have their indications. However, we do not feel that the advantages of the perineal route are generally accepted.[1]

Many advances have been made in the field of prostatic surgery since Dr. George Goodfellow[2] performed the first perineal prostatectomy in 1891. He is accredited with making a success of the perineal operation in America. His operation was a rather crude and blind one as compared with the present procedure. It was not until 1903 that Dr. Hugh Young[3] performed his perineal prostatectomy. He popularized the perineal route in this country with his operation that afforded excellent visualization of the prostatic fossa and avoided all anatomic structures of importance in the perineum. Technical improvements in the Young operation have been few, but they include contributions, such as the infra-anal sphincter approach, plastic repair of the vesical neck, and transverse incision in the prostatic capsule.[4-6]

The perineal operation is a standardized procedure and in our hands is the least shocking of the prostatectomies. It is particularly suitable for the elderly patient who is a poor surgical risk. Because of the high incidence of impotence following the operation, we think it should be limited to the elderly patient or to the patient who has serious medical complications. The procedure has fallen into disrepute in many centers because of the risk of urinary incontinence and rectal injury. We maintain that these complications are almost nil by the revised technic, and in our hands the perineal route offers a safe way to rehabilitate the elderly and debilitated patient with a benign enlarged prostate. The ideal operation technically is one that: (1) respects the anatomical integrity of the urogenital diaphragm with its dreaded complications of dribbling and incontinence; (2) avoids injury to the rectum with its sequelae; (3) preserves the perineal nerves and blood vessels; and (4) insures per primam healing.

We utilize a technic that respects the above structures, giving added safety from operative accidents and postoperative sequelae.

Description of Technic

Under spinal anesthesia and with the patient in an exaggerated lithotomy position, the skin of the genitalia and perineum is cleaned and draped in a sterile manner. A curved incision is made from one ischial tuberosity to the other approximately 2 cm. above the anus. The incision is extended through the subcutaneous tissue, and the ischiorectal fossa is developed just enough to identify the rectal wall and the central tendon of the perineum (Fig 1). To avoid injury to the rectum, this structure should be identified before cutting the central tendon. The central tendon is then separated from the rectum with the index finger and severed with curved scissors (Figs. 2 and 3). The dissection is

*Read before the Section on Urology, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

FIG. 1

Identification of rectum.

FIG. 2

Separation of central tendon from rectum.

continued to the apex of the prostate. At the apex of the prostate the levator ani is gently retracted laterally and the recto-urethralis muscle stands out in the midline (Figs. 4 and 5). With one finger in the rectum to avoid injury to this structure, the recto-urethralis is cut, allowing the rectum to fall back and bringing Denonvilliers' fascia into view. The recto-urethralis is severed close to the rectal wall to avoid injury to the urogenital diaphragm and the urethral bulb. The posterior layer of Denonvilliers' fascia is pushed back from the prostate. A transverse incision is made in the prostatic capsule about 1.5 cm. from the apex. Care must be taken not to make the incision too far back resulting in the anterior flap of the capsule acting as a curtain, obstructing the view of a portion of the prostatic fossa. The original Young's capsular incision was an inverted "V"-shape and often impaired the circulation of the tip of the flap. With the transverse incision, we feel that both flaps have adequate blood supply. The line of cleavage is developed between the adenomatous tissue and the surgical capsule with curved scissors and the enu-

FIG. 3

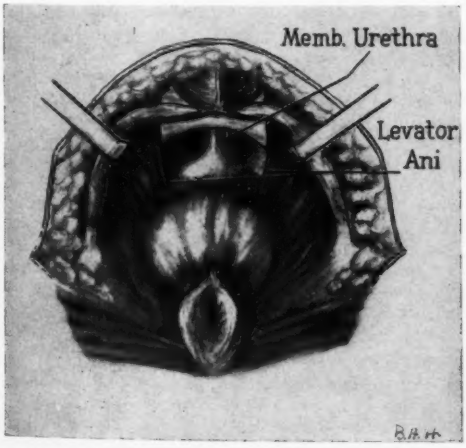
Cutting the central tendon.

FIG. 4

Cutting the recto-urethralis muscle.

cleation is carried out with the short Young prostatic retractor and the index finger. Bleeding at the vesical neck is controlled with No. 0 plain catgut, and capillary oozing in the fossa is controlled with the electrocautery. After adequate hemostasis, a No. 24 Foley catheter is passed and distended with 20 cc. of water. The prostatic capsule is completely closed using a running suture of No. 0 plain catgut. A Penrose drain is placed down to the capsule and the levator ani is loosely approximated in the midline.

FIG. 5



Anatomy of perineum. (Courtesy of Dr. Basil A. Hayes, South. M. J. 48:236, 1955).

At no time during the procedure is the urogenital diaphragm entered; the procedure is carried out with a minimal of bleeding. The entire procedure requires approximately one and one-half hours. The Penrose drain and the urethral catheter are removed on the third day. Rarely is it necessary to reinsert the catheter because of perineal leakage. The patient is always placed on chemotherapy postoperatively and per primam healing is the rule.

The following two cases are cited as evidence of the smooth postoperative convalescence following the perineal operation in elderly patients who are extremely poor surgical risks.

Case Reports

Case 1. This 64 year old married man was brought into the emergency room of the Charlotte Memorial Hospital because of acute urinary retention. He gave a history of progressive obstructive prostatism of at least one year's duration.

Past history revealed he had had a myocardial infarction one year ago. During his convalescence from his cardiac condition, he had a cerebral hemorrhage with resultant right hemiplegia. For the past few months he had been in a nursing home confined to bed and the wheel chair.

The medical consultant considered him too poor a risk for operation and he was returned to the nursing home with an indwelling urethral catheter. His course was followed in the office, and his catheter changed at weekly intervals.

After one month, the patient was readmitted to the hospital because he elected to have an operation rather than to wear a urethral catheter. There was little change in his cardiac status as judged by the EKG, and his right hemiplegia was still present. His NPN was 29 mg. per cent. Urinalysis showed specific gravity 1.011, 2 plus albumin and numerous red and white blood cells on microscopy.

Cystoscopy revealed a markedly trabeculated bladder and two large intraurethral lateral lobes of the prostate. A perineal prostatectomy was done under low spinal anesthesia with continuous oxygen by mask during the procedure. He had a smooth postoperative convalescence. His catheter was removed on the third postoperative day but was reinserted for one day because of perineal leakage. Upon his discharge on the ninth postoperative day the wound had healed nicely and the patient voided with a good stream.

Case 2. This 66 year old married man was first ad-

mitted to the Charlotte Memorial Hospital in 1944, because of acute urinary retention. At that time a transurethral resection of the prostate was carried out. He did fairly well until 1948, at which time he was readmitted to the hospital because of bleeding. Cystoscopy revealed a Grade II prostatic hypertrophy and a transurethral resection was advised but was refused by the patient.

His next admission was in January, 1954, because of recurrent bleeding. A transurethral resection of the prostate was done. Postoperatively the patient went into acute cardiac failure with marked pulmonary congestion necessitating intravenous digitalization and artificial respiration by the anesthesia machine. He was discharged improved on February 8, 1954.

On February 9, 1954, he was readmitted because of recurrent bleeding. It was the opinion of the urologist and also of the medical consultant that the recurrent bleeding was a greater hazard than operation. On February 12, 1954, a perineal prostatectomy was performed under low spinal anesthesia and continuous oxygen therapy. Approximately 56 Gm. of prostatic tissue was removed which showed benign glandular hyperplasia on pathologic examination. The catheter was removed on the third postoperative day and the patient was discharged on the seventh postoperative day. The wound had healed nicely and the patient voided with a good stream. To date he has had no recurrence of his bleeding.

Analysis of 110 Perineal Prostatectomies

Average Age of Patient—74
Average Weight of Gland—50.5 Gm.
Average Postoperative Stay—9.7 days
Anesthesia—Low spinal except with marked pulmonary emphysema.
Complications

1. Postoperative bleeding—4 cases treated with reinsertion of catheter.
2. Incontinence—0
3. Rectal fistula—0
4. Urethral stricture—0
5. Mortality—0

Morbidity

1. Least shocking
2. Marked freedom from suprapubic pain and bladder spasms
3. Ambulatory one postoperative day
4. Abdominal complications rare
5. Per primam healing

Conclusions

In conclusion, we have advocated a revised technic in perineal prostatectomy which avoids injury to the rectum, urogenital diaphragm, perineal nerves and blood vessels. The revised technic is simple, is easily carried out and, in our hands, has prevented postoperative complications and sequelae which have caused the perineal prostatectomy to be unpopular in the hands of many competent urologists.

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Discussion (Abstract)

Dr. Van Scott, Birmingham, Ala. In discussing perineal prostatectomy one is struck by the fact that fifty years after this operation was first introduced it is still necessary to emphasize its value. There is no question but that the operation described by the authors requires a considerable amount of equipment as well as two assistants. For this reason I use the perineal approach to the prostate only for the purpose of obtaining a specimen for biopsy in cases of suspected carcinoma.

The variations in technic advocated by the authors are certainly worthy of consideration. There is no question but that division of the central tendon of the perineum before identifying the rectal wall as is usually done increases the danger of injury to the rectum. Separating the central tendon of the perineum from the rectum with the index finger before dividing it would certainly lessen the possibility of rectal injury. My greatest difficulty in exposing the prostate perineally has been in dividing the recto-urethralis muscle at the apex of the prostate. The insertion of one finger in the rectum to facilitate this dissection seems worthwhile, because it is at this stage of the operation that most rectal injuries occur.

I do not think that the risk of urinary incontinence or rectal injury is great enough to make one discard this procedure, because it is particularly useful in the management of the elderly debilitated patient. I am in complete agreement with the authors that there should be a revived interest in this procedure, especially in the training of young urologists, because not only is the approach of definite value in the removal of benign adenomas of the prostate, but it is the only reliable means by which early carcinoma can be diagnosed. For this reason, all those who treat cancer of the prostate should be familiar with perineal exposure of the gland. Inability or reluctance to expose the prostate perineally for the purpose of biopsy seriously restricts the physician in his management of prostatic cancer, with the result that certain patients receive palliative anti-androgenic treatment rather than curative surgical treatment. I feel very strongly that it should be the obligation of everyone concerned with the training of young urologists to provide adequate training in perineal prostatic surgery.

This contribution of Drs. Justis and McKay should help to overcome prejudice to this procedure and should make the general acceptance of the perineal route a reality.

Dr. Abel J. Leader, Houston, Tex. The authors deserve high praise for their skillful and extremely lucid presentation. I have no fault to find with their conclusions, since I subscribe to them with no reservations. But I was interested in noting that the authors refer to four surgical approaches to the prostate. It is only for the sake of completeness and in order to spare you the embarrassment that was mine when I discovered that there were indeed more than four avenues of approach that I am led to make these remarks.

It was at the bi-annual meeting of the Mexican Urological Congress held in Mexico City in May of 1953 that I was nonplussed to discover that most of the urologists were familiar with an approach referred to as the ischiorectal juxta-sphincteric approach to the adenomatous prostate. I say I was nonplussed because it was my conviction at the time that we in the United States were familiar with about everything that was known about urology. On investigation, I learned that Dr. Eduardo Ortega of Ecuador had taken the oldest of the approaches to the prostate, that of Voelker of Berlin, had modified it, and had demonstrated it in numerous operating theaters in the Latin American countries.

Later, I had the good fortune to meet Dr. Ortega in Chicago at the meeting of the International College of Surgeons, where he had participated in a panel discussion dealing with the surgical approaches to the obstructing prostate. A most gracious and charming gentleman, he accepted my invitation to come to Houston to present a paper, his motion picture on this operative method, and to demonstrate it for the urologists of Southeast Texas. We were quite impressed with all of it.

The principal advantages of this new avenue of attack are said to be two: the lateral approach through the ischiorectal fossa brings into view the lateral margin of the prostatic capsule. Dr. Ortega was readily able to demonstrate the presence of a well-defined neurovascular bundle that courses below the line of incision into the prostatic capsule. By avoiding injury to this structure, the major disadvantages of the perineal approach are overcome: those of urinary incontinence, whether temporary or permanent, and loss of potency, which seems to follow in the majority of cases of perineal prostatectomy. Further, since the rectum is avoided, perforations of that structure are less likely to occur than in the classical perineal approaches of either Young or Belt.

In the one case that Dr. Ortega demonstrated for us, both the operation and the postoperative course proved to be everything he claimed they would be, and we were most impressed. We have since operated upon 9 patients by this method, and it is apparent from our experiences that the method has much to recommend it. Dr. Ortega tells me that his series is now in excess of 200 cases and that it is likely that we shall have a report from him soon at one of the annual meetings of the American Urological Association. You may consider this, then, as a preview of another surgical approach to the prostate that we shall hear more about later. In the meantime, if you should hear the operation mentioned, you will not be as totally unaware of it as I was some two years ago.

HOTEL RESERVATION APPLICATION FORM FOR 50TH ANNUAL SESSION, WASHINGTON, NOVEMBER 12-15, APPEARS IN THIS ISSUE. MAKE YOUR RESERVATION EARLY!

Treatment of Hypertension: Part IV.

Pharmacology and Therapy of Hypertensive Emergencies*

JOHN H. MOYER, M.D., and EDWARD W. DENNIS, M.D.,† *Houston, Tex.*

EFFECTIVE TREATMENT OF HYPERTENSIVE EMERGENCIES requires an agent which will reduce the blood pressure quickly and effectively. It is fortunate that a choice of drugs is available at this time. However, the potency of many of these agents is such that an intimate knowledge of pharmacodynamics of them is necessary if they are to be employed with maximum efficiency and safety. The very potency of many of these agents makes them dangerous if improperly employed.

Marked elevation in blood pressure itself, even though due to many different causes, may become a direct threat to the patient's life if not brought under immediate control. This is so even though the elevated blood pressure may be only a part of the clinical syndrome. Under these circumstances control of the blood pressure can become the primary therapeutic problem and, in fact, can become a life saving procedure. The more important disease entities in which hypertension can become an emergency are acute nephritis, toxemia of pregnancy, hypertensive encephalopathy, pheochromocytoma, fulminating heart failure due to essential hypertension, hypertensive crisis, cerebral hemorrhage with severe hypertension, renal artery occlusion and others. The following report is a general discussion of the therapeutic approach to blood pressure reduction in these disease entities.

General Principles

Although the exact physiology underlying the majority of cases of hypertensive emergencies associated with essential hypertensive vascular disease is not known, the importance of the autonomic nervous system in its maintenance seems well founded (Figs. 22A and 22B). It has been established that drugs which produce a blockade at various points along the sympathetic pathways from the higher centers to the neuro-effector site will, among other effects, reduce the blood pressure in these instances. It has been observed also that certain of these compounds are capable of reducing the arterial blood pressure regardless of the degree of its elevation and without regard to the underlying cause of the hypertension. Initial preparations which were introduced for treating severe hypertension were variable in their effect and somewhat difficult to control. Although there have been many refinements, no ideal drug has yet been developed which makes it mandatory that the pharmacodynamics of the more potent agents be understood if serious side reactions are to be avoided.

The blood pressure can be reduced by suppression of vasoconstrictor impulses at their

TABLE 1

BLOOD PRESSURE RESPONSE OF 17 PATIENTS WITH SEVERE FIXED HYPERTENSION—CONTINUOUS INFUSION OF VERILOID

	Control	*Veriloid*
Blood Pressure		
Systolic (mean)	243	156*
Diastolic (mean)	159	107*
Pulse rate (mean)	88	69*

*Statistically significant ($P < 0.01$) change from control value.

TABLE 2

CLINICAL RESPONSE TO CONTINUOUS INFUSIONS OF VERILOID—17 PATIENTS WITH SEVERE HYPERTENSION AND ENCEPHALOPATHY

Side Reactions	*Number Patients*
None	5
Nausea with	12
Vomiting	4
Hiccough	4
Marked weakness	4
Dizziness	2
Symtomatic Improvement	
None	4
Minimal	2
Moderate	4
Marked	7

*Read before the Section on Medicine, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

†From the Departments of Medicine and Pharmacology, Baylor University College of Medicine, Houston, Tex.

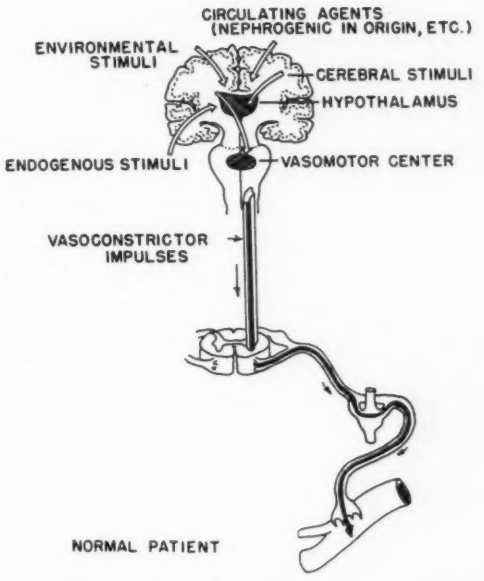
Supported in part by the Houston Heart Association.

sites of origin (central blockade), or blockade of the vasoconstrictor impulses along their transmission pathway either at the ganglion or at the sympathetic nerve ending. The pharmacologic agents which are used in the treatment of hypertensive emergencies may be classified on the basis of their sites of action within the sympathetic nervous system (Fig. 23). The most effective centrally acting agents are Rauwolfia, veratrum and hydralazine which suppress vasoconstrictor impulses at their sites of origin at or above the vasoregulatory centers. Ganglionic blocking agents, i.e., hexamethonium, pentolinium and mecamylamine, act not only at sympathetic ganglia to block vasoconstrictor impulses but also at the parasympathetic ganglia to produce a variety of effects. The third major group of autonomic blocking agents are those which produce adrenergic blockade at the neuro-effector site (Fig. 23) and are of value only for the short term control of hypertensive crises associated with pheochromocytoma prior to surgical extirpation of the tumor. Although each of these groups of agents is effective in reducing the blood pressure, each can produce a variety of untoward effects in addition to the desired reduction in blood pressure. Side effects so produced are usually predictable if the mechanism of their action is understood.

In treating hypertension, one presupposes that by reducing the blood pressure, damage to the three key vascular beds, i. e., the brain, the heart and the kidneys, may be reduced or reversed. Most of the symptoms and altered bodily functions resulting from prolonged or severe hypertension may be attributed to damage of these three important beds. Similarly, each must be kept in mind during treatment if therapeutically induced complications are to be avoided. Smirk[7] has concluded that if hypertension reaches a sufficient degree of severity and is sustained for an adequate period of time, this in itself is an intermediate cause responsible for the clinical manifestations which are associated with all hypertensive diseases.

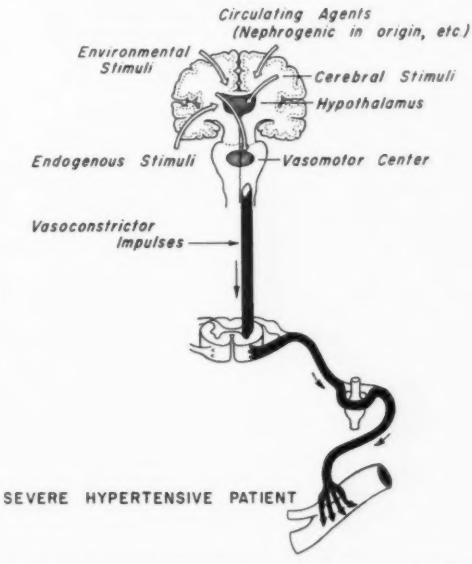
Cerebral function is improved by lowering the blood pressure in hypertensive patients particularly if hypertensive encephalopathy exists (Table 2).[27] When the blood pressure is reduced, the cerebral vessels dilate and

FIG. 22, A



Diagrammatic representation of vasoconstrictor impulses originating in the brain and traveling to the blood vessels in a patient with normal blood pressure. (Courtesy Am. J. M. Sc. 230:33, 1955).

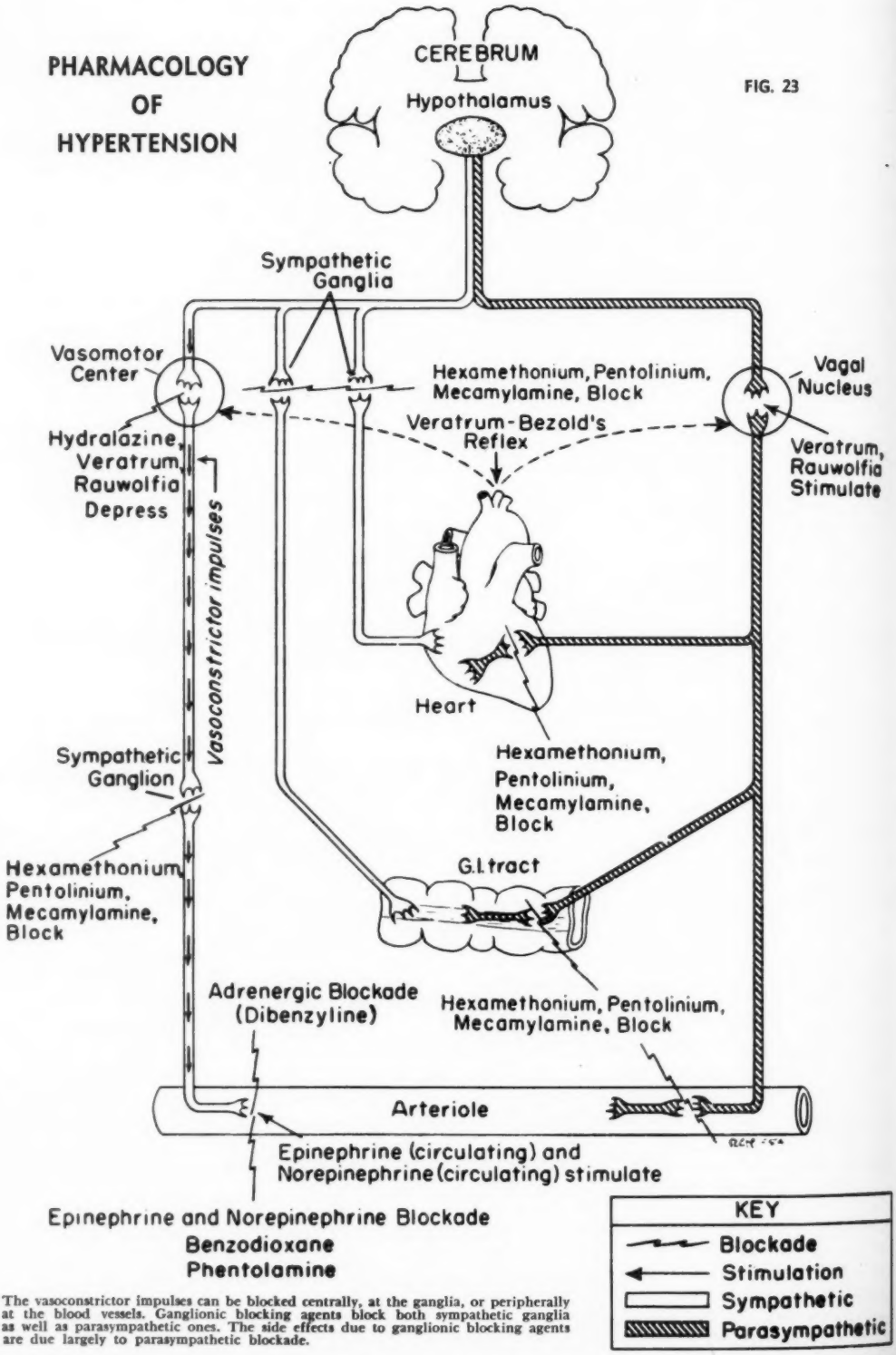
FIG. 22, B



In the patient with severe hypertension there is marked increase in outflow of vasoconstrictor impulses over the sympathetic nervous system to the blood vessels, or an increase in response to the normal impulses reaching the blood vessels. This produces vasoconstriction with a marked rise in blood pressure. As the blood pressure remains markedly elevated for prolonged periods of time it produces secondary vascular damage. (Courtesy Am. J. M. Sc. 230:33, 1955).

PHARMACOLOGY OF HYPERTENSION

FIG. 23

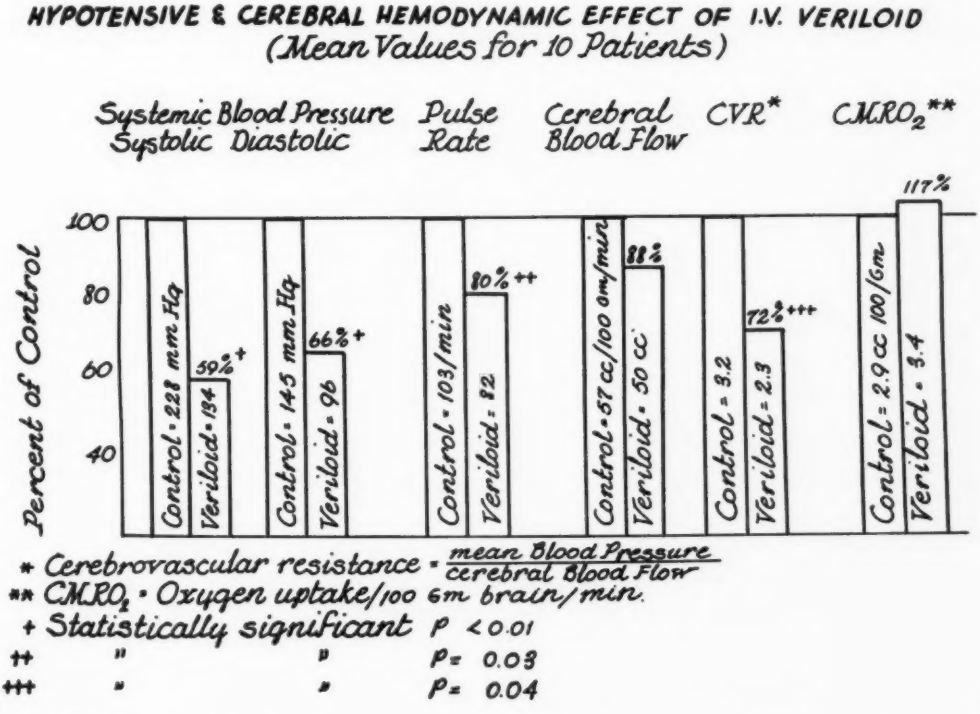


The vasoconstrictor impulses can be blocked centrally, at the ganglia, or peripherally at the blood vessels. Ganglionic blocking agents block both sympathetic ganglia as well as parasympathetic ones. The side effects due to ganglionic blocking agents are due largely to parasympathetic blockade.

cerebral blood flow and metabolism are maintained (Fig. 24). If the blood pressure is reduced excessively, however, cerebral blood flow may decrease sharply (Fig. 25). This is frequently observed in the upright position when agents acting at the ganglion or peripheral to it are used, since reflexes responsible for adjusting peripheral vascular resistance to compensate for position change may be inhibited with resultant excessive hypotension in the upright position. When this occurs dizziness in the upright position may be prominent. In treating moderate to severe hypertension with peripherally acting agents in the ambulatory patient, one should not seek to achieve normotensive levels in the supine position but should adjust the dose of the drug by the upright blood pressure determinations. An upright blood pressure of 150/100 appears to be safe.

In regard to the myocardial blood supply, the improvement in intractable angina pectoris suggests that the ratio of coronary blood flow to metabolic demand is improved when the blood pressure is reduced with Rauwolfia, veratrum or ganglionic blocking agents. Generally, cardiac failure is improved following reduction of blood pressure, and catheter studies by British investigators have shown a significant reduction of pressure in the pulmonary artery and right ventricle following ganglionic blockade.[9] On the contrary hydralazine, by increasing the heart rate, may produce palpitation, angina and even myocardial infarction[8] when it is used alone (Figs. 26A-26C) in the presence of coronary artery disease. This agent should be given parenterally to young individuals only, such as patients with toxemia of pregnancy and acute glomerular nephritis. The tachycardia resulting from the administration of hydralazine is minimized if parenteral reserpine or gan-

FIG. 24



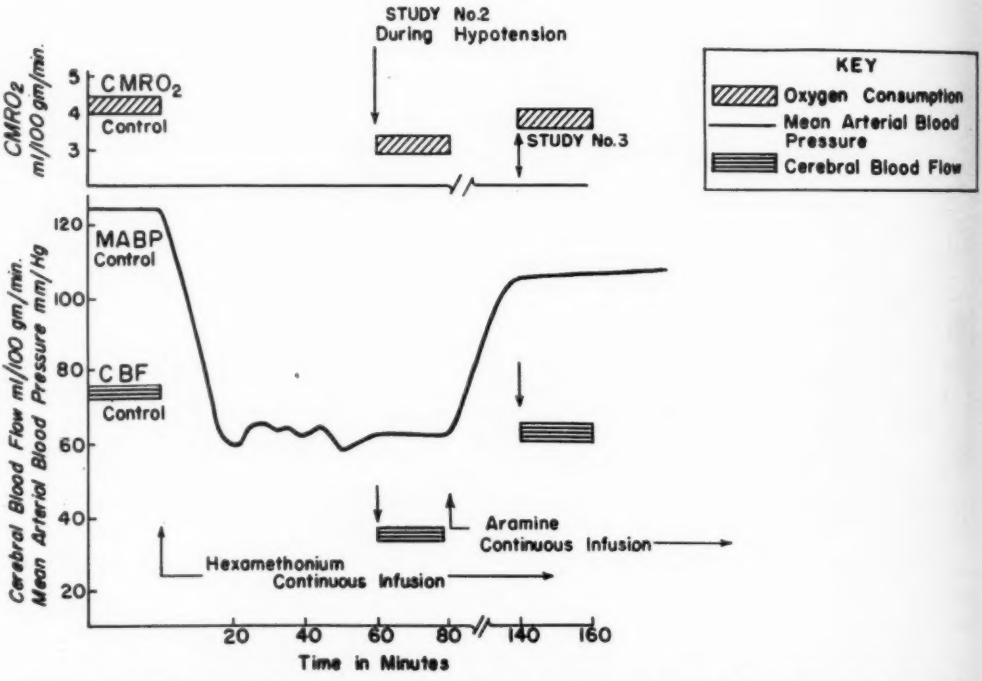
As the blood pressure is reduced with potent antihypertensive agents (Veriloid [alkavervir]) administered parenterally, cerebrovascular resistance decreases and cerebral blood flow is maintained unless the blood pressure is reduced to low normotensive or hypotensive levels. When the latter occurs cerebral blood flow decreases concurrently. (Courtesy Am. J. Med. 14:175, 1953).

glionic blocking agents are administered first.

As a generalization, if pretreatment renal function is not significantly impaired, glomerular filtration rate and renal blood flow are reduced only slightly, even though renal vascular resistance decreases following reduction of blood pressure by autonomic blockade. One exception to this rule is hydralazine which temporarily increases renal blood flow but does not alter or may reduce glomerular filtration rate. Following acute reduction in blood pressure, renal function is depressed more by the ganglionic agents than by the centrally acting agents. During continuous intravenous infusion (Figs. 27A-27C) of ganglionic blocking agents, glomerular filtration rate and renal blood flow are depressed and remain depressed throughout the period of infusion to patients with hypertension. However, after intermittent parenteral administration there is a similar initial depression in renal function following which renal blood flow tends to return to control levels (Fig. 27A) despite a persistent depression in glomerular filtration rate. There is essentially no difference in the response to pentolinium or hexamethonium (Fig. 27C). In patients with severe pretreatment hypertension and associated renal disease, the reduction of the blood pressure must be approached cautiously. Following prolonged intermittent parenteral or oral administration of these agents, the glomerular filtration rate gradually returns to normal despite a maintained reduction in blood pressure (Fig. 5)* if this is not excessive. Patients with renal damage respond qualitatively similarly to patients with normal kidneys, but the readjustment is slower and incomplete.[10] If readjustment is incomplete and if renal function is markedly impaired, even small reductions in glomerular filtration may be serious enough to decompensate the kidney and cause renal failure. Incomplete renal hemodynamic

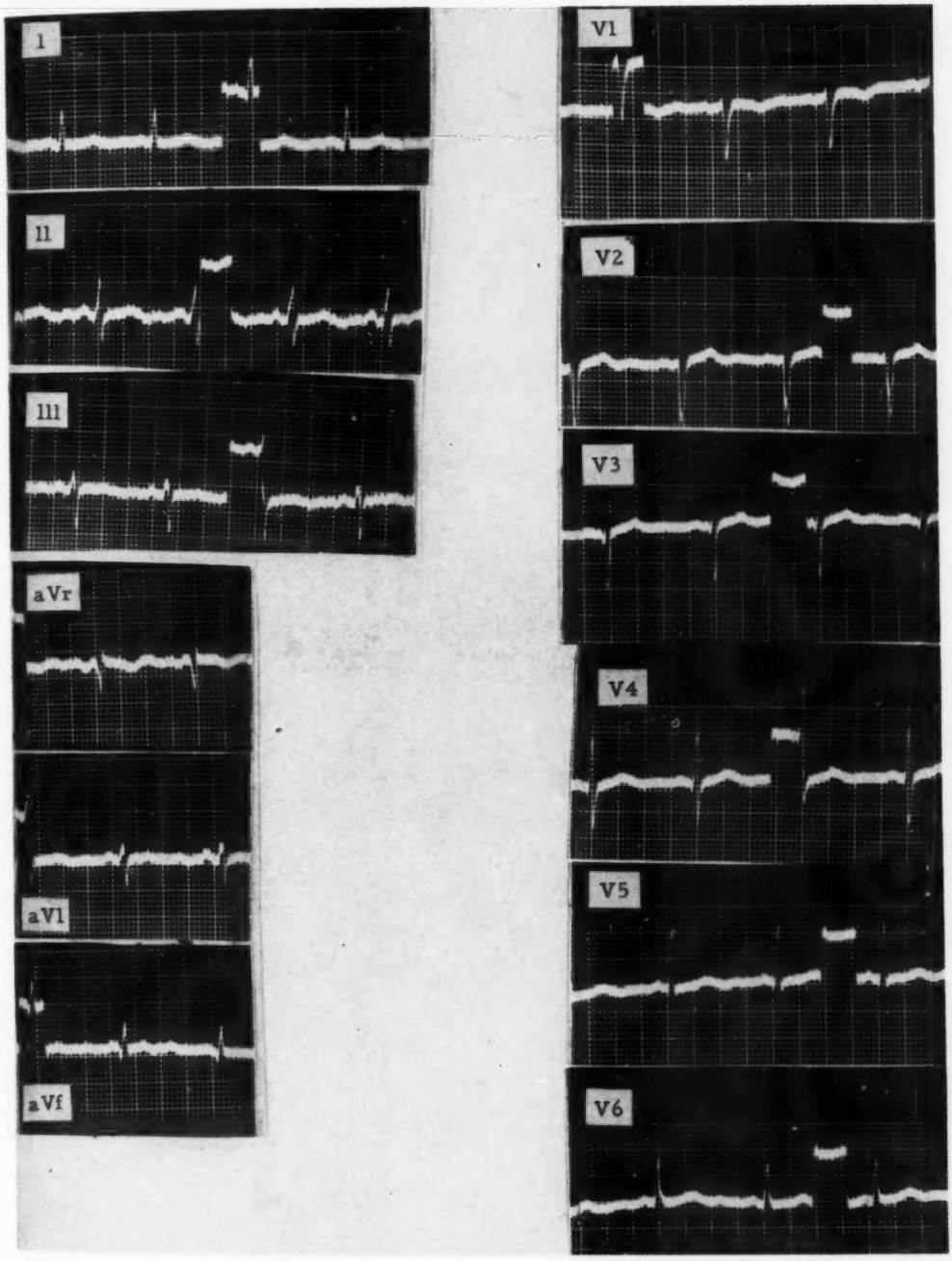
*Dennis, Edward W., and Moyer, John H.: Treatment of Hypertension: Part I. Pathogenic Considerations and Older Methods of Therapy, South. M. J. 48:1251, 1955.

FIG. 25



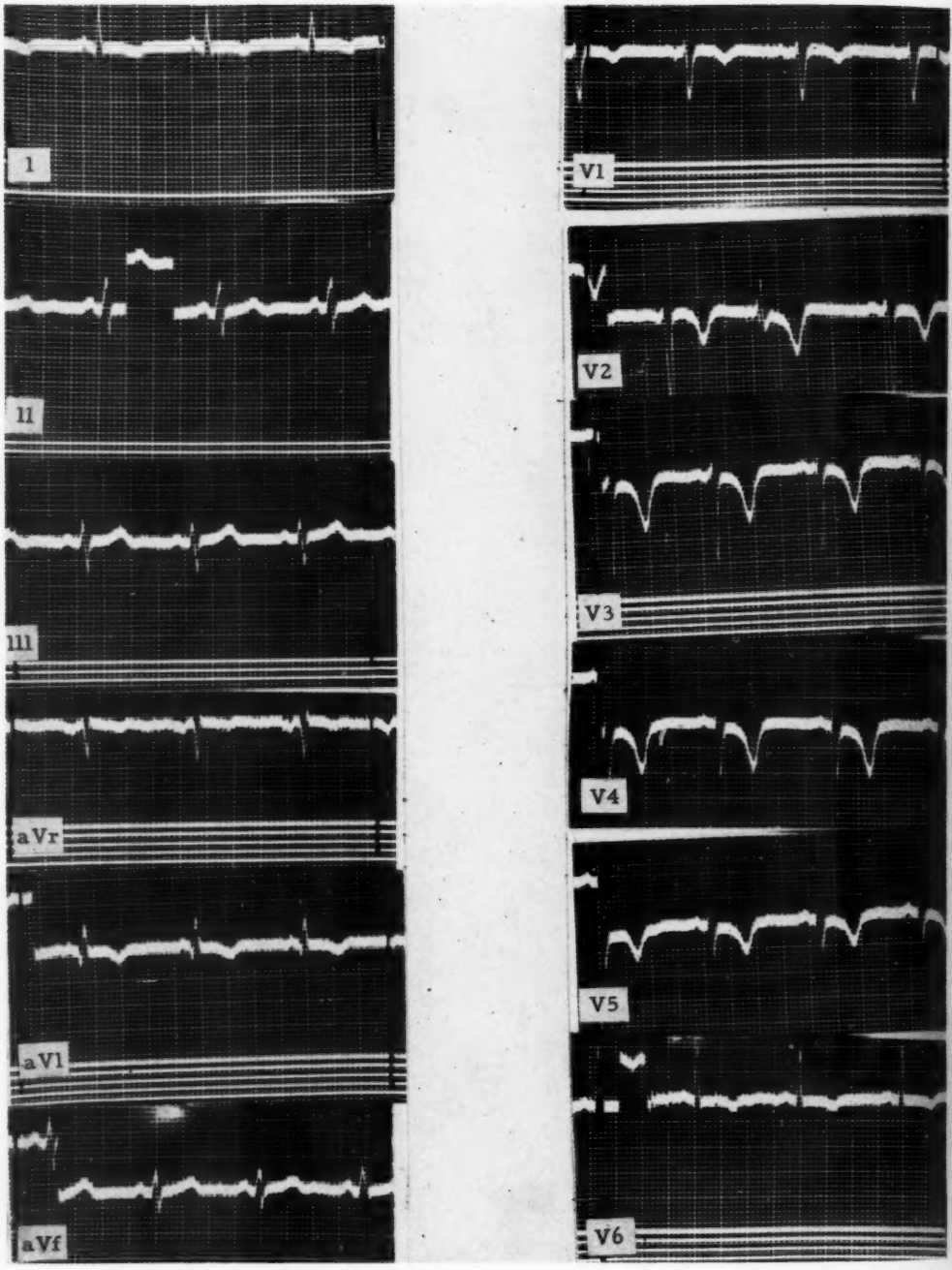
The effect of blood pressure (MABP) reduction to hypotensive levels on cerebral blood flow (CBF) and cerebral oxygen uptake ($CMRO_2$). As the blood pressure decreases cerebral blood flow is reduced. When the blood pressure is again raised to normotensive levels, cerebral blood flow returns toward the control value. (Courtesy J. Clin. Invest. 33:1081, 1954).

FIG. 26, A



Electrocardiograms in a patient who developed marked tachycardia and chest pain 30 minutes after ingestion of 150 mg. of hydralazine (Apresoline). (Courtesy A.M.A. Arch. Int. Med. 91:419, 1953).
(A) During the control period there was evidence of minimal coronary artery disease prior to the administration of hydralazine.

FIG. 26, B



(B) EKG taken 3 days after hydralazine showed evidence of acute myocardial infarction.

FIG. 26, C

(C) EKG 6 months later indicates improvement.

readjustment is more likely to occur if the blood pressure is reduced to absolute normotensive or hypotensive levels (Fig. 28). This means that when blood pressure reduction is undertaken, particularly in persons with serious renal disease, extreme care must be taken in order to maintain the standing blood pressure slightly above normotensive levels. Frequent determinations of the blood urea nitrogen must be carried out. An increase in the degree of nitrogen retention should constitute a contraindication to lowering the blood pressure to a greater degree.

In all patients with severe hypertension, a careful evaluation of the cerebral, cardiac and renal status must be carried out before the initiation of therapy. Not only will the plan of approach and immediate goal of treatment depend on this, but also it is only through alteration in the status of these three vascular beds that evaluation of beneficial and untoward results may be made.

Centrally Acting Agents

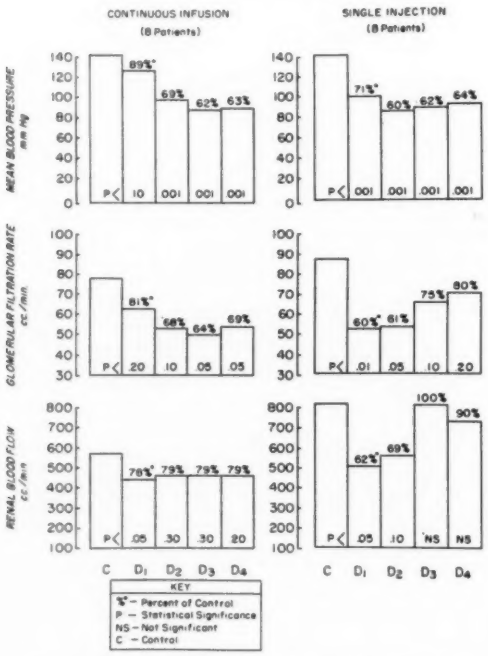
*Reserpine**. When given parenterally in adequate doses, reserpine (a pure alkaloid of *Rauwolfia serpentina)* is probably the most useful antihypertensive agent available for the treatment of hypertensive emergencies. Administered parenterally it is quite potent in contrast to the response to the same drug after oral administration. However, there is a latent period of one to two hours before the blood pressure decreases, following either intravenous or intramuscular administration. Therefore, if immediate reduction in blood pressure is required a more rapidly acting drug is indicated. Under these circumstances, either a ganglionic blocking agent or a veratrum extract** may be used initially and the reserpine administered at the same time for its long-term effect. Following the initial re-

*Available as Serpiloid by Riker Laboratories, Inc., and as Serpasil by Ciba Pharmaceutical Products, Inc.

**In the case of pregnancy toxemia or acute nephritis, hydralazine seems to be more effective.

FIG. 27, A

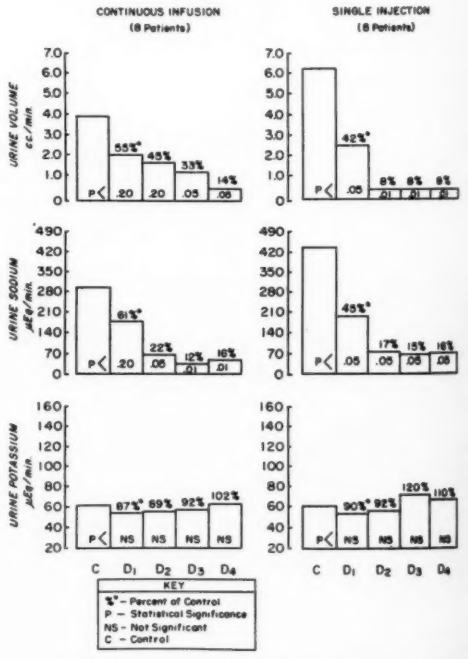
EFFECT OF INTRAVENOUS PENTOLINIUM ON RENAL HEMODYNAMICS IN HYPERTENSIVE PATIENTS



Renal hemodynamic response to acute blood pressure reduction with pentolinium given by continuous infusion as compared to intermittent parenteral administration.

FIG. 27, B

EFFECT OF INTRAVENOUS PENTOLINIUM ON WATER AND ELECTROLYTE EXCRETION IN HYPERTENSIVE PATIENTS



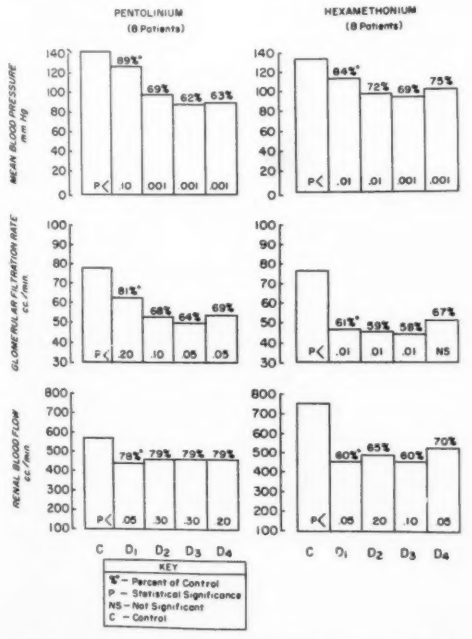
Effect of acute blood pressure reduction on water and electrolyte excretion.

duction in blood pressure with the ganglionic blocking agent or veratrum, the patient can frequently be maintained with reserpine alone.

We have studied this drug in three different groups of patients. These include hypertensive emergencies associated with, (1) severe essential hypertension (Figs. 29A and 29B), (2) toxemia of pregnancy (Fig. 36), and (3) severe hypertension of renal origin such as acute nephritis (Fig. 30) and patients with a "Goldblatt" kidney (Fig. 31). The results achieved in these patients indicate that reserpine, administered parenterally, is a relatively potent antihypertensive agent. It seems that there are few hypertensive patients who do not obtain a significant reduction in blood pressure. The antihypertensive effect is manifested in the recumbent as well as in the upright position, an attribute of considerable importance in acutely ill and bed-fast patients. The decrease in blood pressure is slow and the relatively rare instance of excessive hypotension permits effective and safe therapy, without the necessity for constant bedside attendance by medical and nursing personnel. The treatment of hypertensive emergencies with reserpine given by the parenteral route would seem to be most useful on a short-term basis, after which effective medication may be administered orally. This conversion is relatively simple since the control of blood pressure achieved with parenteral reserpine is lost slowly after the reserpine is discontinued. This allows time for establishing an effective program of oral drug therapy without a loss in blood pressure control (See Parts I, II and III of this review).

FIG. 27, C

EFFECT OF CONTINUOUS INTRAVENOUS PENTOLINIUM vs HEXAMETHONIUM ON RENAL HEMODYNAMICS IN HYPERTENSIVE PATIENTS



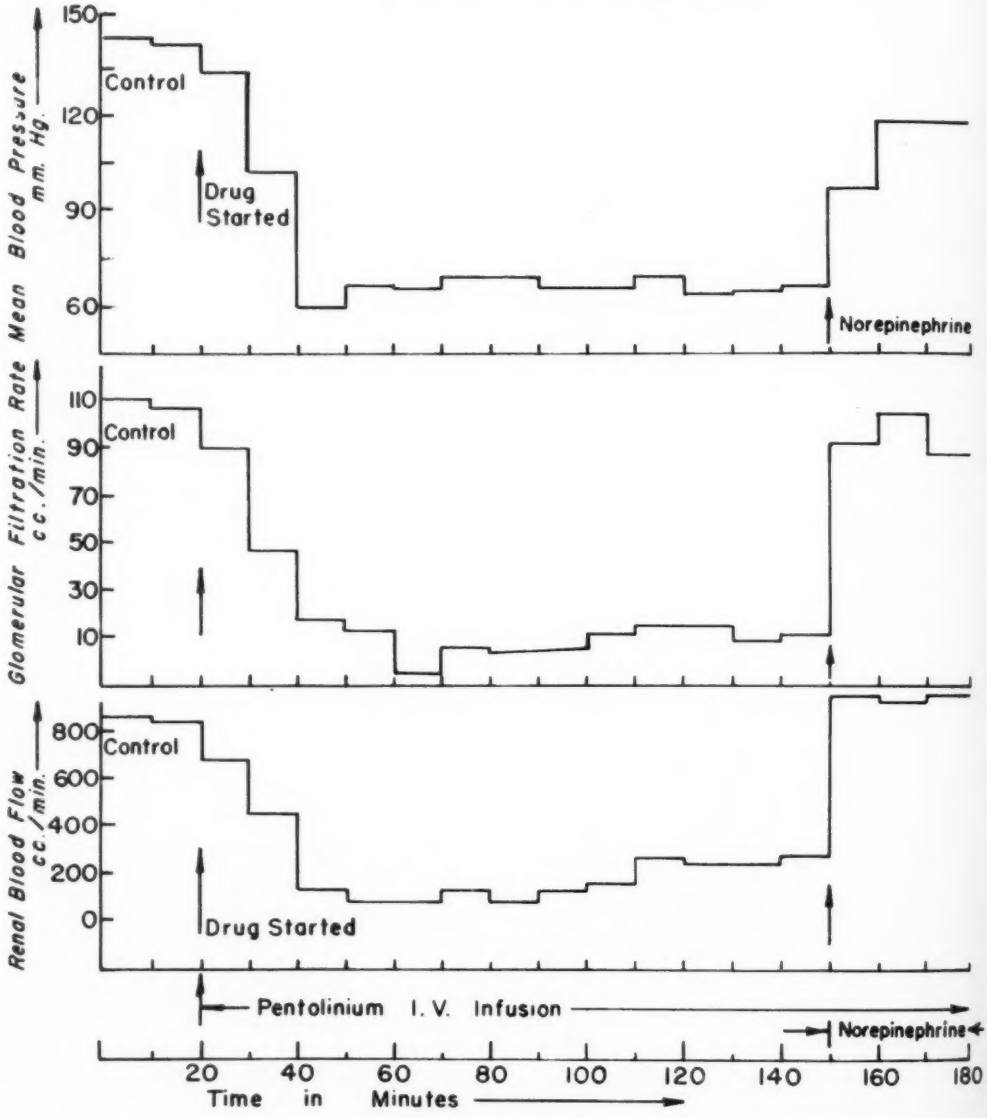
Renal hemodynamic response to a continuous infusion of pentolinium as compared to hexamethonium. (Courtesy Am. J. M. Sc. 231:294, 1956).

Administration: The procedure for administration of reserpine parenterally in these patients is best determined on the basis of the initial blood pressure response (Fig. 29A) to 5 to 10 mg. of reserpine. The drug may be administered intramuscularly, or it can be given intravenously in 100 cc. of 5 per cent glucose given over a 15 to 30 minute period. This response varies in degree and duration in different patients. The patients are then placed on a regular schedule which usually consists of 5 to 10 mg. of reserpine given every 6 to 12 hours (Fig. 29B). The maintenance dose and the interval between doses is adjusted so as to maintain the desired blood pressure levels. Norepinephrine is an effective antidote and should be used if excessive reduction in blood pressure occurs, which is rare. Blood pressure, pulse rate and respiration should be recorded every 30 minutes following the initial doses and as necessary following subsequent doses.

The side effects tend to become more prominent as either the dose or the frequency of administration of reserpine is increased. Tolerance to the sedative effect usually becomes evident after a few days of therapy but an increase in the dose will usually elicit more sedation again. Muscle tremors and other manifestations suggesting a Parkinson's syndrome may appear if doses of 5 to 10 mg. are given as frequently as every 4 hours, but these disappear slowly after a decrease in the dose, or frequency of administration, or after discontinuation of therapy. Conjunctival injection is prominent.

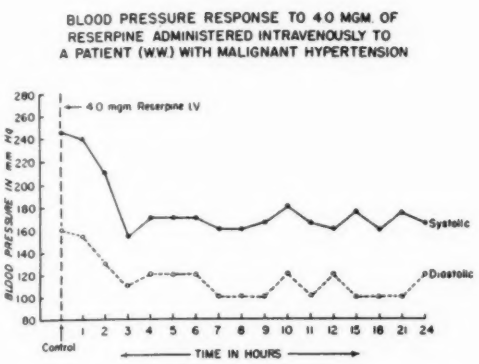
FIG. 28

Renal Hemodynamic Response to Excessive Reduction in Blood Pressure With Pentolinium



Renal hemodynamic response to excessive reduction in blood pressure with pentolinium. As the blood pressure was reduced to hypotensive levels glomerular filtration decreased from 111 c.c. to less than 10 cc. per minute. At the same time renal blood flow was reduced to less than 100 cc. per minute. As blood pressure remained down renal function remained depressed. However, when the blood pressure was increased to normotensive levels with norepinephrine, glomerular filtration rate and renal blood flow returned toward normal despite a maintained ganglionic blockade.

FIG. 29, A


BLOOD PRESSURE RESPONSE TO 4.0 MGM. OF RESERPINE ADMINISTERED INTRAVENOUSLY TO A PATIENT (W.W.) WITH MALIGNANT HYPERTENSION
4.0 mgm. Reserpine I.V.
BLOOD PRESSURE IN mm. Hg
Systolic
Diastolic
Control
TIME IN HOURS

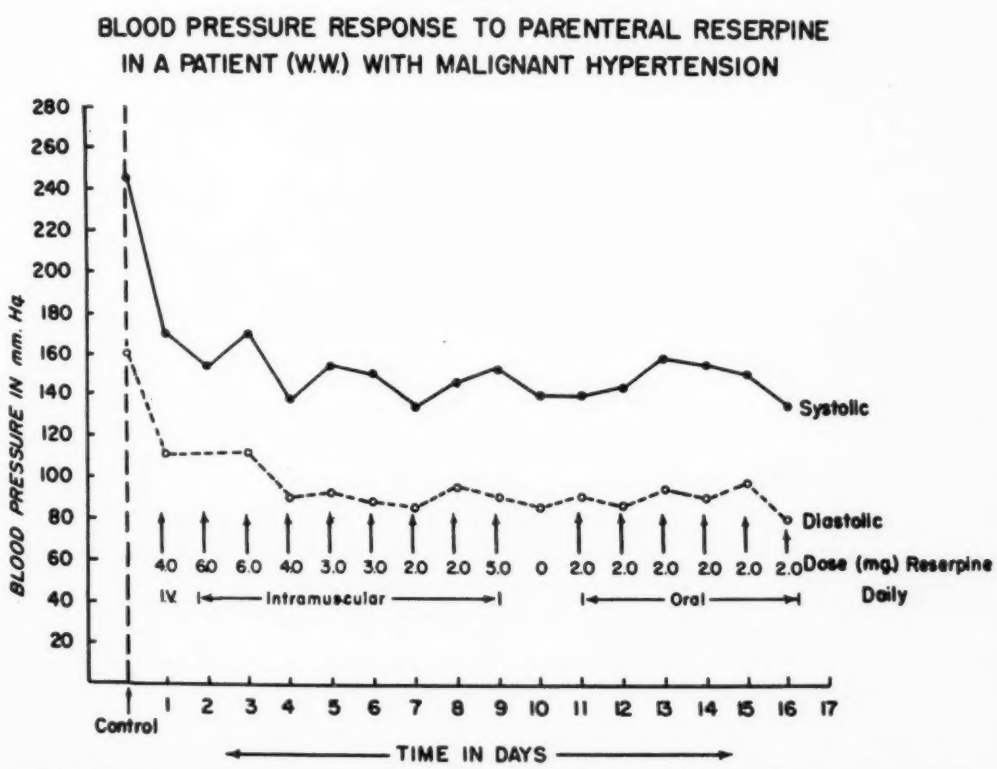
A patient with malignant hypertension. (Courtesy A.M.A. Arch. Int. Med. 95:563, 1955). (A) The blood pressure response to 4 mg. of reserpine administered intravenously. Onset of significant blood pressure reduction occurred 2 hours after injection, and maximum reduction occurred at 3 hours. Significant blood pressure effect still present after 24 hours.

In a group of 10 patients with malignant hypertension, all of the patients obtained a significant reduction in blood pressure and 70 per cent became normotensive. In a group of 100 patients with toxemia of pregnancy, all but 11 responded adequately. The remaining 11 responded when hydralazine was given in addition to the reserpine. In a third group of patients of pediatric age with acute glomerular nephritis, 7 of 8 patients obtained an adequate reduction in blood pressure (Fig. 30) but in one patient the disease progressed rapidly and death occurred before an adequate reduction in blood pressure could be obtained.

*Rescinnamine.** This is another pure alkaloid obtained from *Rauwolfia serpentina* and is similar to reserpine. When given parenter-

*Supplied as Rescinnamine by Riker Laboratories, Inc.

FIG. 29, B


BLOOD PRESSURE RESPONSE TO PARENTERAL RESERPINE IN A PATIENT (W.W.) WITH MALIGNANT HYPERTENSION
BLOOD PRESSURE IN mm. Hg
Systolic
Diastolic
4.0 6.0 6.0 4.0 3.0 3.0 2.0 2.0 5.0 0 2.0 2.0 2.0 2.0 2.0 2.0 Dose (mg.) Reserpine Daily
I.V.
Intramuscular
Oral
Control
TIME IN DAYS

(B) The blood pressure response during therapy with parenteral reserpine and after one week after conversion to the oral route. The blood pressure was maintained quite consistently at normotensive or mild hypertensive levels. One week following discontinuation of parenteral reserpine, pentolinium was added because of the gradual loss of adequate reduction in blood pressure.

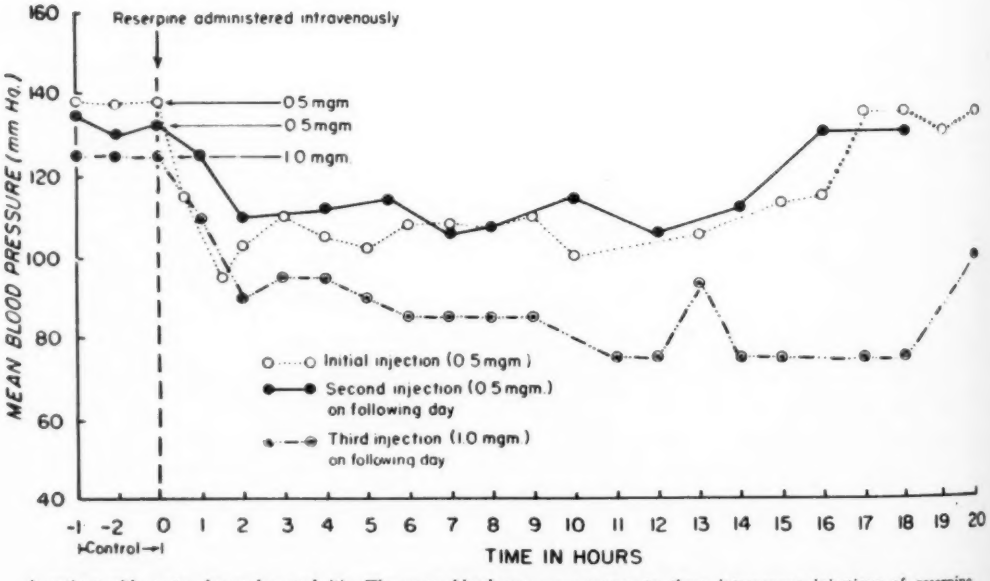
ally, Rescinnamine is equally as effective as reserpine (Fig. 32) but the dose required is 1.5 to 2 times as great. There is essentially no difference in the incidence and severity of side effects of reserpine as compared to Rescinnamine except that somnolence is less marked with the latter. The manner of administration is the same for both agents.

*Alkavervir.** Parenteral alkavervir, a veratrum extract, is one of the most potent centrally acting vasodepressor agents which can be given either intramuscularly or by continuous intravenous infusion. The onset of action is rapid, i. e., within 10 to 20 minutes. When using this drug great caution must be exercised because the blood pressure can easily be lowered excessively. In our experience, the veratrum alkaloids are the most potent antihypertensive agents available for general use. In addition to the effect on the blood pressure, the drug produces a rather marked reduction in pulse rate by vagal stimulation. It may also produce nausea and vomiting in many cases in which an effective reduction in blood pressure has been obtained. The incidence of side effects is high (Table 2) when adequate amounts of this agent are used to reduce the blood pressure to normotensive levels (Table 1). For example, in a study conducted by the authors, (Table 2) nausea and/or vomiting was observed in 12 of 17 patients so treated. Despite the high incidence of side reactions, some improvement in the encephalopathic manifestations exhibited by these patients was observed in all but 4 patients and in 7 of the 17 cases, all manifestations of encephalopathy cleared following an effective and maintained reduction in blood pressure.

*Supplied as Veriloid by Riker Laboratories, Inc.

FIG. 30

BLOOD PRESSURE RESPONSE TO INTRAVENOUS RESERPINE IN A PATIENT (O H.) WITH ACUTE GLOMERULO-NEPHRITIS



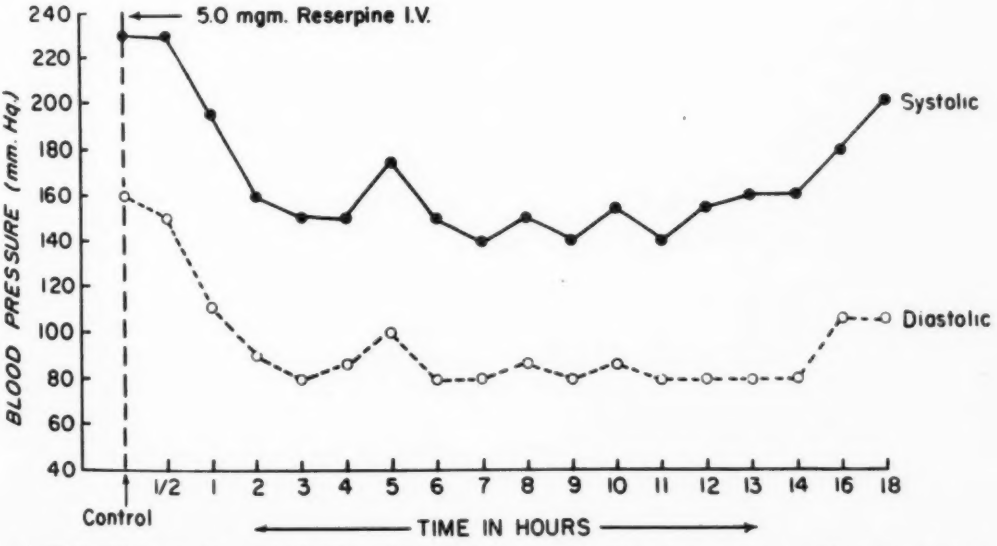
A patient with acute glomerular nephritis. The mean blood pressure response to three intravenous injections of reserpine is shown. Hypertensive levels were present at the time of each injection. The same characteristics of blood pressure response occurred after each injection, indicating that reserpine was responsible for the blood pressure depression. (Courtesy A.M.A. Arch. Int. Med. 95:563, 1955).

Method of Administration: When used intravenously, an initial priming dose of alkavervir is given, which consists of giving 0.5 microgram per kilogram body weight per minute over a 20 minute period (Fig. 33). The blood pressure should be checked every minute during this time and until an adequate reduction in blood pressure is obtained. A change is then made to the sustaining infusion (Fig. 34). The priming dose is prepared by diluting 10 micrograms per kilogram body weight of intravenous solution of alkavervir in 10 cc. of 5 per cent glucose in distilled water. If the desired hypotensive effect has not been achieved with the initial priming dose, it may be repeated at least in part. The sustaining solution consists of 4 mg. of alkavervir added to a liter of 5 per cent glucose in distilled water. This is given at a rate which is regulated depending on the amount necessary to maintain the desired blood pressure level.

As a safety precaution, a similar infusion containing 4 mg. of norepinephrine per liter of 5 per cent glucose in distilled water should be prepared beforehand and connected through a "Y" tube (Fig. 34) for immediate infusion should the blood pressure decrease excessively at any time. Norepinephrine is a very effective antidote. During the initial infusion of alkavervir or protoveratrine (a pure veratrum alkaloid), the blood pressure and pulse rate should be checked every two minutes for the first 30 minutes and then every 5 minutes for the full stabilizing period. The blood pressure should be checked every 15

FIG. 31

BLOOD PRESSURE RESPONSE TO 5 MGM. OF RESERPINE ADMINISTERED INTRAVENOUSLY TO A PATIENT (G L M) WITH MALIGNANT HYPERTENSION ASSOCIATED WITH OCCLUSION OF THE ABDOMINAL AORTA AND LEFT RENAL ARTERY

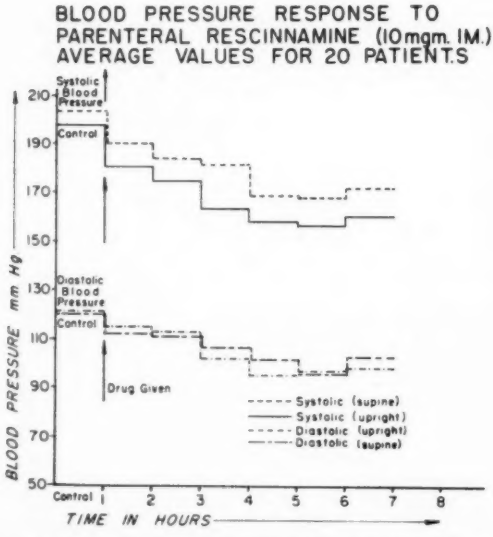


A patient with hypertension associated with renal ischemia following unilateral renal artery occlusion. Blood pressure was reduced with parenterally administered reserpine just as in the case of essential hypertension. This case represents the clinical counterpart to the "Goldblatt kidney" which can be produced in the laboratory. (Courtesy A.M.A. Arch. Int. Med. 96:518, 1955).

to 20 minutes throughout the entire period of intravenous infusion of alkavervir. This requires the full-time attendance of a nurse or someone well trained in the use of these drugs who is capable of taking blood pressures properly. As soon as feasible, oral and intramuscular hypotensive therapy should replace the intravenous infusion.

When the route of administration of alkavervir is changed from the intravenous to the intramuscular one, the first intramuscular dose should be 0.6 mg. given every 4 to 6 hours (Figs. 35A and 35B). The dose should then be increased in 0.2 mg. increments until significant reduction in blood pressure occurs, after which the dose should be increased more gradually, usually in about 0.1 mg. increments until the blood pressure is reduced to the desired level. Then the frequency of administration is adjusted depending upon the length of action of the drug as reflected in the length of time the pressure remains reduced. The blood pressure should be recorded at least every 15 minutes until the dose is well adjusted following intramuscular administration of the drug. Norepinephrine or a similar vasopressor agent should be available at the bedside at all times in the event that excessive hypotension occurs. Atropine, in a dose of 1 mg. is very effective in combating excessive bradycardia. There is no effective antidote for the nausea and vomiting that may be associated with veratrum.

FIG. 32



Blood pressure response to parenteral rescinnamine. Essentially the same type and degree of response that would be observed following the administration of parenteral reserpine. (Courtesy Am. J. M. Sc, In Press).

*Hydralazine.** Hydralazine is of limited value in the treatment of hypertensive emergencies and is confined primarily to use in acute glomerular nephritis and toxemia of pregnancy in which disease entities it enjoys some specificity of action. Best results are obtained when this drug is used in conjunction with reserpine. The onset of reduction in blood pressure (15 to 20 minutes) is more rapid after hydralazine than after the administration of reserpine. Therefore, it is given in cases where rapid onset of action is necessary, or to patients who do not respond adequately to reserpine alone.

Method of Administration: In toxemia of pregnancy, 5 to 10 mg. of reserpine are given concurrently or preceding the hydralazine. The frequency of reserpine injection for optimum effect has been found to be at 6 to 8 hour intervals; this is governed by blood pressure response.

Hydralazine is best given intravenously to these patients either as a single injection of 10 to 20 mg. or as continuous intravenous infusion of 20 to 50 mg. diluted in 1,000 cc. of 5 per cent dextrose in water. The continuous infusion method is more desirable in most cases where the blood pressure is quite labile, i.e., during labor. Although most patients will respond to reserpine alone, hydralazine should be added to the regimen when a more rapid effect is desired and/or when a more marked fall in blood pressure is desired. While hydralazine alone is effective in these patients, reserpine counteracts the tachycardia produced by hydralazine, aids in maintaining the normotensive state, and also provides sedation. Hydralazine may be of value to patients with renal disease because of its renal vasodilating property, although this response is temporary.

Hydralazine will precipitate acute hypertensive crises in patients with a pheochromocytoma (Fig. 37). Although the agent depresses the vasoregulatory areas in the brain and thus reduces the blood pressure, it ap-

*Supplied as Apresoline by Ciba Pharmaceutical Products, Inc.

parently stimulates other components of the sympathetic nervous system such as the cardioaccelerator area. This is manifested by a consistent increase in pulse rate following the parenteral administration of hydralazine. There is very little peripheral blocking effect (adrenergic blockade) of this drug in doses used clinically since, within this dose range, no adrenergic blockade or norepinephrine blockade is observed. For example, in figure 37 is shown a patient with a pheochromocytoma in whom an acute hypertensive response followed the administration of hydralazine. If this agent had been capable of blockade of norepinephrine, this increase in blood pressure would not have occurred even though the norepinephrine had been liberated into the blood stream.

Ganglionic Blocking Agents

The three most useful ganglionic blocking agents which can be given either intravenously or intramuscularly for the treatment of hypertensive emergencies are hexamethonium, pentolinium (Ansolysen)* or mecamylamine (Inversine).** These drugs must be given by a titration procedure by means of which the dose is individualized for each patient.

Hexamethonium.† When giving hexamethonium intravenously, 100 mg. are given in an intravenous preparation in 1,000 cc. of 5 per cent glucose in distilled water. The drug is

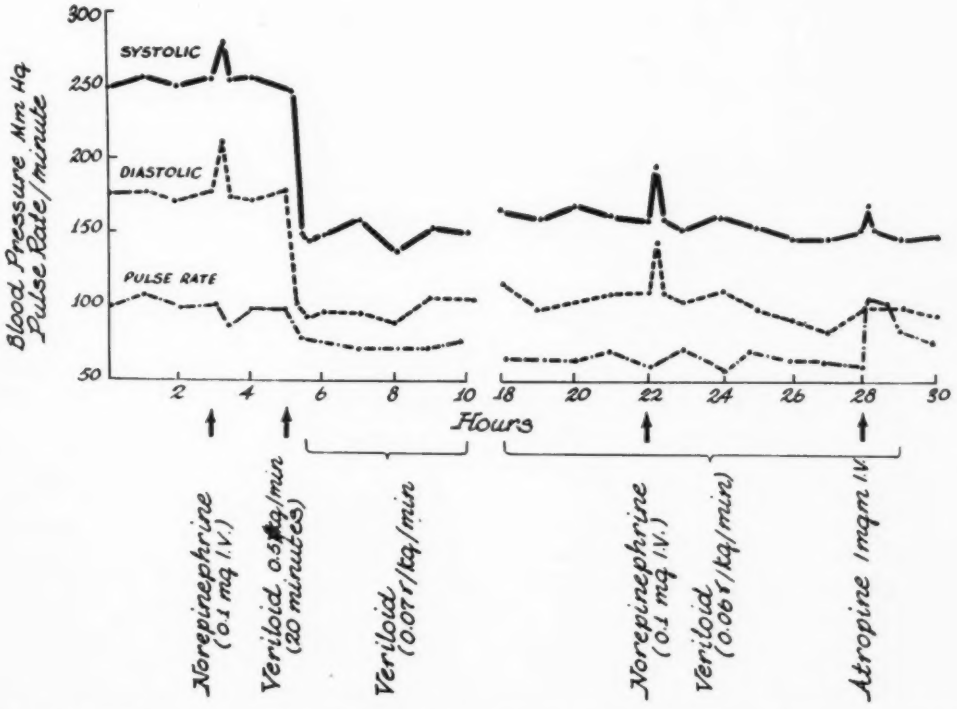
*Supplied as Ansolysen by Wyeth Laboratories.

**Supplied as Inversine by Sharp & Dohme, Division of Merck & Co.

†Supplied as Methium by Warner Chilcott Laboratories and Esomid by Ciba Pharmaceutical Products, Inc.

FIG. 33

CONTINUOUS INFUSION OF VERILOID INTRAVENOUSLY

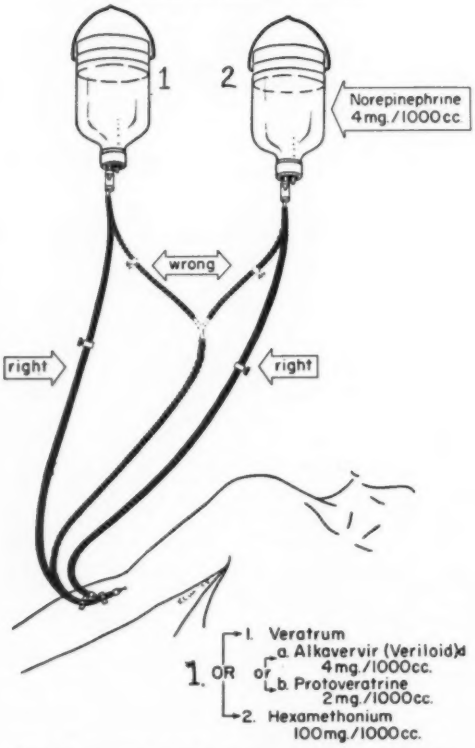


A typical response to intravenous alkavervir (Veriloid). Pulse rate and systolic and diastolic blood pressure all decreased concurrently. Atropine blocks the bradycardia but displays only an insignificant and transient effect on blood pressure. The blood pressure response to a single dose of intravenous norepinephrine is just as marked after and during Veriloid administration as it is during the control study. (Courtesy Am. J. Med. 14:175, 1953).

infused at a moderate rate until the blood pressure begins to fall, then the rate of infusion is adjusted so as to maintain an adequate reduction in blood pressure. As a safety precaution the infusion apparatus should be connected to a Y-tube such as in figure 34. Norepinephrine is an effective antidote for hexamethonium as well as all other ganglionic blocking agents in the event that excessive reduction in blood pressure should occur, since these agents block at the level of the ganglia whereas norepinephrine acts peripherally directly on the blood vessels. The blood pressure and pulse rate should be checked at least every 5 minutes during the initial period of adjustment. After the blood pressure has been stabilized it should be checked at least every 15 to 20 minutes. If inadequate reduction in blood pressure is obtained, the response can usually be enhanced if the head of the bed is elevated.

FIG. 34

APPARATUS FOR CONTINUOUS INFUSION OF VERATRUM OR HEXAMETHONIUM



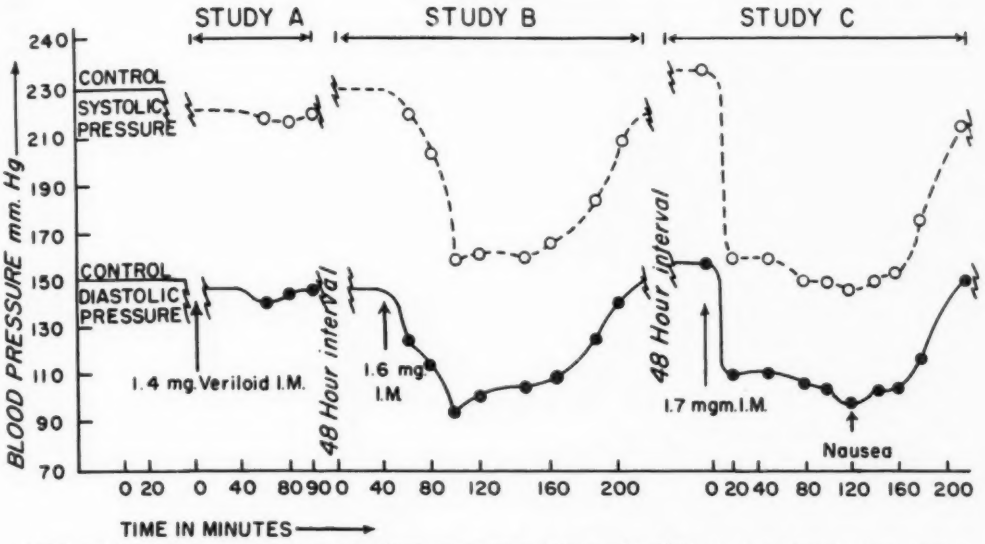
Method for setting up the apparatus for continuous intravenous infusion of veratrum or ganglionic blocking agents. (Courtesy M. Rec. & Ann. 49:438, 1955).

When administering hexamethonium intramuscularly, the initial dose is 15 mg. After waiting one hour to determine the effect of the initial dose, another dose is given and subsequent doses are given in increasing increments until an adequate effect is obtained. Usually, the drug can be repeated every one to two hours until effective reduction in blood pressure occurs. Doses in excess of 100 mg. are usually no more effective than this amount. Hexamethonium, when given intramuscularly, is a safe and effective agent and the danger of excessive reduction in blood pressure is not as great as with veratrum. The frequency of administering intramuscular hexamethonium will depend on the length of time that the blood pressure remains reduced after each injection. Usually, it is only necessary to give the drug every 4 to 6 hours. As soon as the hypertensive emergency is under control the patient should be started on oral therapy as outlined in our previous communications in this series. Care must be exercised in reducing the blood pressure in patients with renal failure lest the renal function be impaired further. A systolic blood pressure of 170 to 180 mm. Hg. is usually a safe level.

Pentolinium. Pentolinium is used in essentially the same manner as hexamethonium. When making up the intravenous infusion, however, 50 mg. is adequate. This amount is placed in 1,000 cc. of 5 per cent glucose and the rate of infusion adjusted according to the blood pressure response. When giving the drug intramuscularly an initial dose of 5 mg. is used. After one to two hours, the second dose is given and so on until an adequate reduction in blood pressure is obtained. Usually, the second dose is 10 mg. and the doses are progressively increased until the blood pressure has been adequately controlled or a maximum of 50 mg. per dose is given. If the blood pressure is not reduced adequately with 50 mg. or less, given intramuscularly, it is rarely possible to obtain an increased response with doses in excess of this amount. The same problems exist with this drug as have been noted in the use of hexamethonium (Figs. 38A and 38B).

If the blood pressure is reduced excessively, glomerular filtration rate in the kidneys is

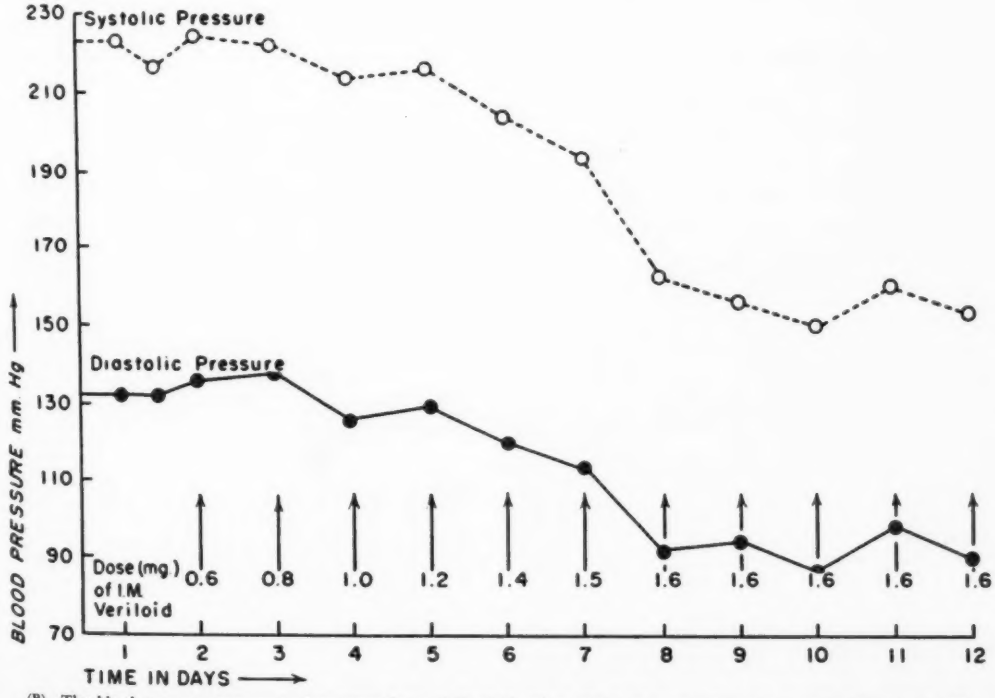
FIG. 35, A



Method and blood pressure response to intermittent intramuscular injection of Veriloid. (A) At a dose of 1.4 mg. there is a minimal blood pressure response. The maximal tolerated response was obtained at a dose of 1.7 mg. given every 4 hours. (Courtesy Am. J. M. Sc. 226:477, 1953).

FIG. 35, B

BLOOD PRESSURE RESPONSE TO A TITRATED DOSE OF INTRAMUSCULAR VERILOID (AQUEOUS SOLUTION) WITHOUT PREVIOUS ORAL THERAPY



(B) The blood pressure response to increasing doses of Veriloid. These blood pressure values are average values over a 24 hour period.

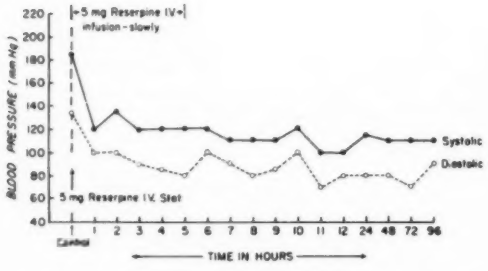
depressed markedly. Since the drug is excreted primarily by the kidney, the drug will be excreted very slowly and the excessive hypotension will last indefinitely if not corrected. Therefore, it is necessary to administer a vasopressor agent and return the blood pressure to high normotensive levels (Fig. 28). This is accomplished readily with norepinephrine, or any other readily available vasopressor agent which can be given intravenously or intramuscularly. The deleterious effect of excessive reduction in blood pressure is even more marked in the presence of renal damage.

Mecamylamine (Inversine). This drug is a secondary amine which is completely absorbed from the gastrointestinal tract and consequently is as effective when given orally as when given parenterally. Therefore, when the patient is capable of taking medication orally, he can be given the same dose by this route as was found to be effective previously when given by the parenteral route. Complete absorption also allows reproducible blood pressure responses to equal doses of drug with minimum day to day variation, which is a serious drawback to ganglionic blocking agents of the quaternary ammonium variety such as hexamethonium and pentolinium.

Method of Administration: This is the most potent ganglionic blocking agent available for clinical use. The initial dose is 3 mg. given intramuscularly or subcutaneously. This can

FIG. 36

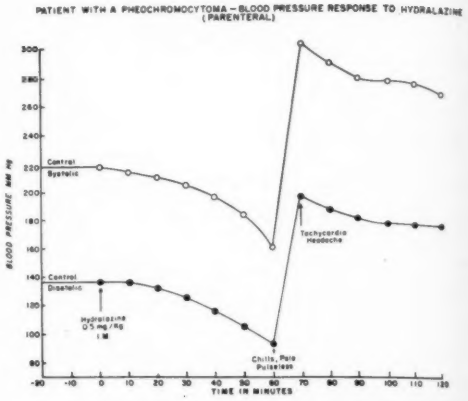
BLOOD PRESSURE RESPONSE TO 10 MG. RESERPINE ADMINISTERED INTRAVENOUSLY TO A PATIENT (I.B.) WITH SEVERE PREECLAMPSIA



A patient with severe preeclampsia. This pateint did not respond to bed rest and sedation. Five mg. of reserpine were given intravenously followed by a slow intravenous infusion containing 5 mg. The blood pressure decreased to normotensive levels one hour after initial injection and remained normotensive.

FIG. 37

PATIENT WITH A PHEOCHROMOCYTOMA — BLOOD PRESSURE RESPONSE TO HYDRALAZINE (PARENTERAL)



Blood pressure response to parenteral administration of hydralazine in a patient with a pheochromocytoma. Following initial reduction in blood pressure a hypertensive crisis was precipitated by the administration of hydralazine. (Courtesy A.M.A. Arch. Int. Med. 91:419, 1953).

be repeated every two hours and increased in 3 to 5 mg. increments until adequate reduction in blood pressure is obtained. Doses in excess of 50 mg. produce no additional effect and should not be given. Tilting the bed in the head-up position assists in reducing the blood pressure. The frequency of administration will depend on the length of time the drug remains effective, frequently 12 to 18 hours.

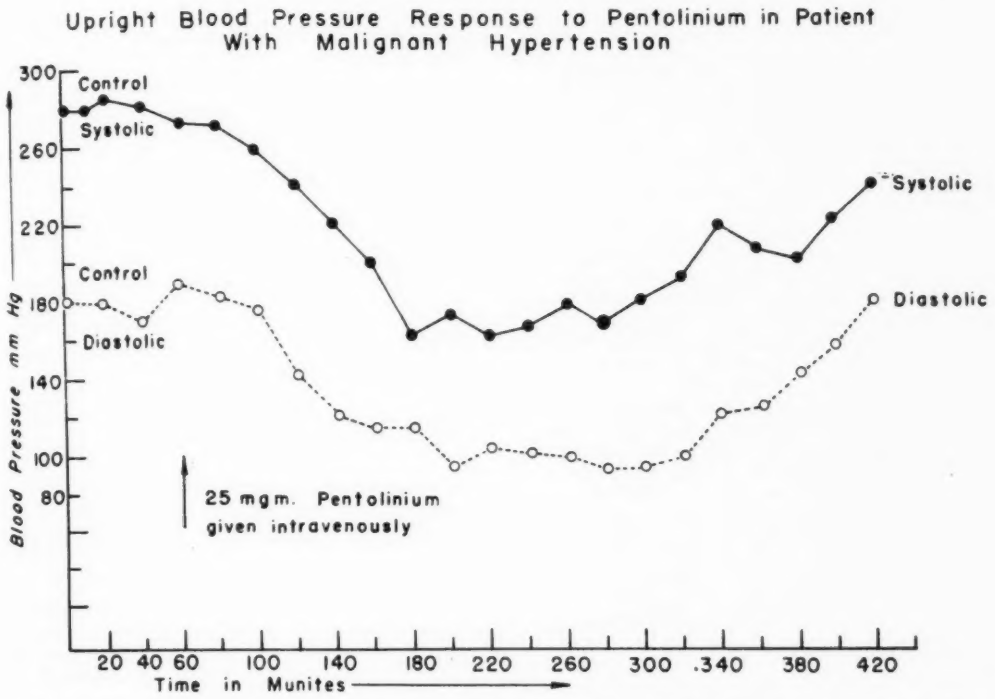
As with pentolinium and hexamethonium, if the blood pressure is reduced excessively, glomerular filtration rate in the kidneys is markedly depressed. Therefore, when this occurs it is necessary to administer a vasopressor agent such as norepinephrine, returning the blood pressure to high normotensive levels.

Peripherally Acting Agents

Phenoxybenzamine (Dibenzyline)* is an effective adrenergic blocking agent which can be given intravenously. However, because of the complete blockade (i.e., both humoral and at the end organ) produced by this drug, rendering vasopressor agents ineffective, it is generally thought inadvisable to administer this blocking agent by the parenteral route. Should excessive reduction in blood pressure occur with the use of this agent, no effective antidote is available.

*Supplied as Dibenzyline by Smith, Kline & French Laboratories.

FIG. 38, A



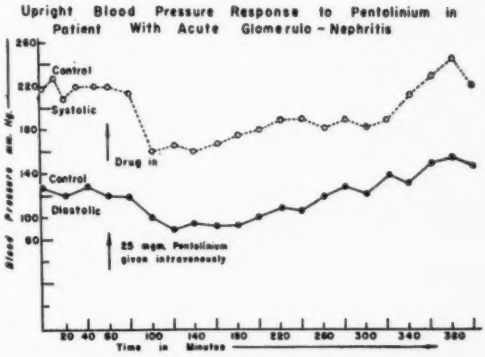
The blood pressure was reduced following the administration of a ganglionic blocking agent quite similar to the response to centrally acting agents such as reserpine except that the reduction in blood pressure was more marked in the upright position.

Phentolamine (Regitine) is useful for the treatment of patients with severe hypertension due to the liberation of norepinephrine by pheochromocytomas. When used for this purpose, it is administered as a temporary measure for controlling the blood pressure prior to and during surgical removal of the tumor. Five mg. of phentolamine is given intravenously or intramuscularly and is repeated as frequently as necessary in order to control the blood pressure. If for any reason the patient must be treated for prolonged periods, the blood pressure can usually be controlled with phenoxybenzamine given by the oral route. The initial dose of phenoxybenzamine by this route is 10 mg. given every 6 hours. The dose is then subsequently increased in 10 mg. increments until effective reduction of the blood pressure is obtained. This method of therapy should be considered a temporary expedient only since this is a curative disease and the tumor should be surgically removed as soon as possible.

Case Reports

Case 1. T. H., (Fig. 39) a 38 year old white man, was admitted to the hospital complaining of excruciating headaches and shortness of breath. He was men-

FIG. 38, B



Ganglionic blocking agents are less effective in reducing the blood pressure in patients who have hypertension secondary to renal disease. Here also the reduction in blood pressure is primarily in the upright position. (Courtesy M. Rec. & Ann. 49:438, 1955).

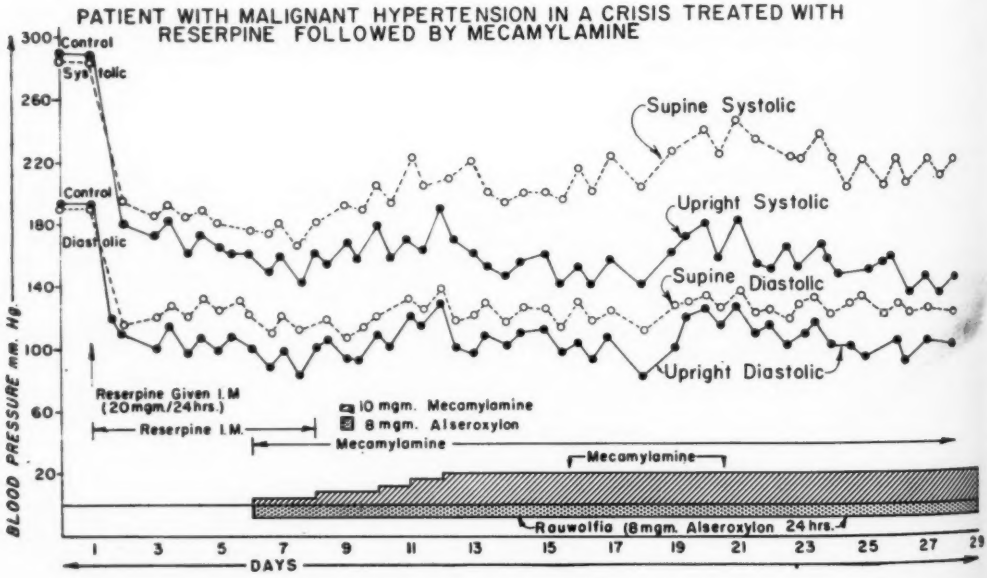
tally confused and markedly ataxic. On physical examination the blood pressure was 290/188 in both the supine and the upright positions. Funduscopic examination revealed marked retinal hemorrhages and papilledema. There was no evidence of a recent cerebral vascular accident having occurred, although the patient showed generalized muscular incoordination. Laboratory examination showed a blood urea nitrogen of 35 mg. per 100 cc. The hemogram was normal. The urinalysis showed numerous red blood cells and granular casts. Albuminuria was present but there were no white cells.

The patient was given 5 mg. of reserpine intramuscularly to which he responded quite well and the blood pressure decreased to 180 mm. Hg. systolic and 100 mm. Hg. diastolic. The reduction in pressure was slightly more marked in the upright position than when the patient remained supine. A single dose of reserpine was effective for a period of 6 hours following which it was necessary to repeat the dose so that the patient required 20 mg. of reserpine each 24 hour period, i. e., 5 mg. every 6 hours. He was continued on this regimen for a period of 6 days after which he was started on oral therapy in addition to the parenterally administered reserpine. Alseroxylon was given in divided doses of 2 mg. four times a day. At the same time, mecamylamine was started in a dose of 5 mg. twice a day. This regimen was continued for 2 days following which the intramuscular reserpine was discontinued and the oral mecamylamine and alseroxylon* (Rauwolfia) were continued. The mecamylamine was increased to 5 mg. after each meal and at bedtime. Thereafter, the dose of mecamylamine was gradually increased to a maximum of 50 mg. per day according to the titration procedure previously described. At the same time, the patient was permitted to get up and about. It is apparent from figure 39 that the blood pressure remained well controlled when the patient was in the upright position but in the supine position it increased to moderately severe hypertensive levels. However, despite the elevation in pressure in the recumbent position, the patient improved rather dramatically, the eye grounds improved and the retinal hemorrhages and papilledema completely cleared. After 4 weeks of antihypertensive therapy the patient was completely ambulatory and all of the encephalopathic manifestations were lost. The blood urea nitrogen was 20 mg. per 100 cc. The patient was then discharged. Two months later, he returned to full-time employment as a postal clerk. He has continued on the same dosage regimen of alseroxylon and mecamylamine that he was receiving at the time of discharge from the hospital.

*Supplied as Rauwiloid by Riker Laboratories, Inc.

Case 2. D. L., (Fig. 40) a 52 year old colored man, was admitted to the hospital in semicoma although the blood urea nitrogen was only 38 mg. per 100 cc. He had had known hypertension for the past 6 months but complained of severe headaches for only one month. Two weeks before admission he noticed blurring of vision and became completely blind in his right eye two days prior to admission. At the time of the initial examination in the hospital the patient was irrational, thrashing around in bed and required restraints. On physical examination, blood was noted throughout

FIG. 39



Diagrammatic representation of therapy and blood pressure response in Case 1.

the vitreous of the right eye and many small punctate hemorrhages were noted in the retina of the left eye. Papilledema was marked. The blood pressure was 280 systolic and 180 diastolic. Urinalysis showed numerous red blood cells and 3+ albuminuria. There were no white cells in the urine.

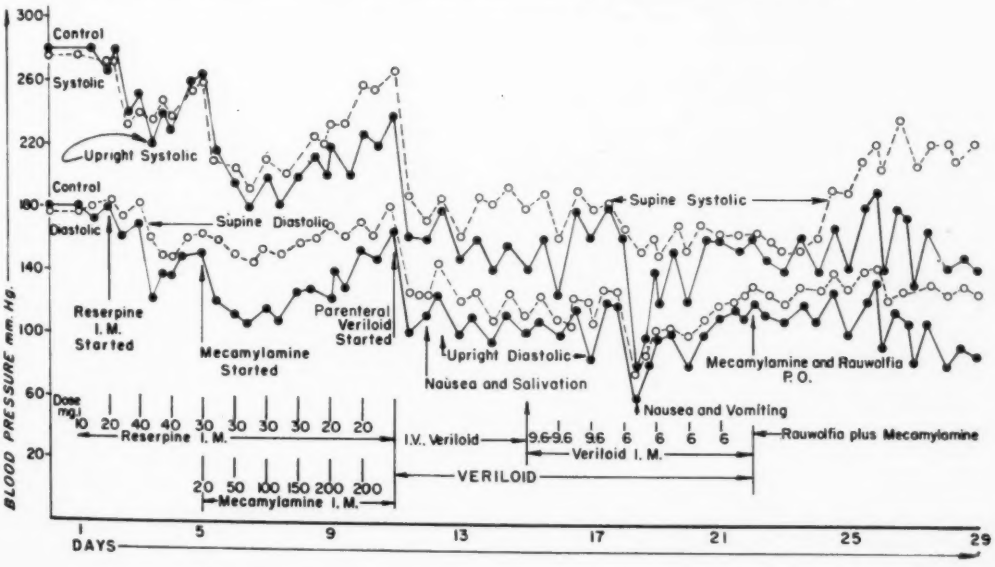
The patient was given 5 mg. of reserpine intramuscularly but he obtained very little reduction in blood pressure. He was then given 10 mg. following which the blood pressure was reduced to approximately 230 systolic and 145 diastolic in the upright position. Because this was considered an inadequate reduction in blood pressure, the reserpine was continued and mecamylamine was given in addition, starting with 10 mg. intramuscularly and gradually increasing the dose to a maximum of 200 mg. per 24 hours in 4 divided doses of 50 mg. each. The dose of reserpine was not increased because the dose of 30 mg. per day produced obvious cerebral depression. With the combination of reserpine and mecamylamine a moderately effective orthostatic reduction in blood pressure was obtained for a period of 5 days (Fig. 40).

However, after this period of time, the blood pressure gradually increased again even in the upright position and it became necessary to administer Veriloid by the intravenous route. This was done according to the method described in the text and a prompt reduction in blood pressure was obtained. It was necessary to continue the intravenous infusion for a period of 4 days during which time the blood pressure was well controlled although nausea and salivation were seen quite frequently. The intravenous Veriloid was then discontinued and the drug was given by the intramuscular route which produced adequate control of the blood pressure. On one occasion an excessive reduction in pressure occurred associated with nausea and vomiting. The dose of Veriloid was then decreased from 9.6 mg. per day to 6 mg. with adequate regulation of the blood pressure and without nausea and vomiting. After 7 days of intramuscular Veriloid therapy, the patient was started on Rauwolfia and mecamylamine given by the oral route. The patient could be adequately controlled on this regimen although the reduction in blood pressure was primarily an orthostatic one. However, as the patient became ambulant the blood pressure was fairly well controlled in the upright position, the retinal hemorrhages cleared and papilledema was reversed. The patient was discharged on the thirtieth hospital day on a daily dose of 1 mg. of reserpine and 150 mg. of mecamylamine. On follow-up one month later, this patient continues to be regulated at about the same level that he was on discharge from the hospital. The urinalysis is now negative and the blood urea nitrogen is 15 mg. per 100 cc. It is believed that this patient will eventually be returned to full-time employment.

The above case history demonstrates that in patients with severe hypertension it is easier to regulate the blood pressure after it has been effectively reduced than it is to regulate it initially during the hypertensive

FIG. 40

MALIGNANT HYPERTENSIVE ENCEPHALOPATHY—UNRESPONSIVE TO RESERPINE AND MECAMYLAMINE—TREATED WITH VERATRUM, GIVEN PARENTERALLY.



Diagrammatic representation of blood pressure response to therapy in Case 2.

crisis. Although mecamylamine was only temporarily effective at the height of the crisis, after his blood pressure was controlled for a period of three weeks it was possible to put this patient on Rauwolfia and mecamylamine again following which a fairly effective reduction in blood pressure was obtained in the upright position.

Summary and Conclusions

1. Hypertensive emergencies can be treated effectively with drugs blocking vasoconstrictor impulses to the blood vessels. These can be divided into centrally acting agents, ganglionic blocking agents, and adrenergic blocking agents.

2. The most useful drugs for treating hypertensive emergencies are the centrally acting agents and the ganglionic blocking agents.

3. The easiest drug to use is reserpine which can be given intramuscularly or intravenously. When inadequate response to reserpine is obtained in patients with acute nephritis or toxemia of pregnancy, hydralazine should be given by the parenteral route.

4. When reserpine is ineffective in patients with essential hypertensive crisis associated with serious complications due to elevated blood pressure, a ganglionic blocking agent such as hexamethonium, pentolinium or mecamylamine should be used either alone or in combination with reserpine. If these are also ineffective, one can then use intravenous alkavervir or protoveratrine. Parenterally administered veratrum extracts (alkavervir or protoveratrine) are the most potent antihypertensive agents available today and it is only rarely that a patient will not respond to these drugs. However, because of their potency and the difficulty of regulation of the blood pressure with these agents, they should be used only in those patients who do not respond to the more simple methods of treatment.

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1-18, inclusive, see South. M. J. 48:1253, (Nov.) 1955.
19-50, inclusive, see South. M. J. 48:1376, (Dec.) 1955.
51-60, inclusive, see South. M. J. 49:85, (Jan.) 1956.

Discussion (Abstract)

Dr. Sidney Schnur, Houston, Tex. I believe first that Dr. Moyer should be congratulated on the clarity and simplicity of this presentation which could have been quite involved, and secondly he and his group deserve the thanks of those of us in practice for their diligent investigation of these many drugs which constantly bombard us. Their purpose has been to clinically evaluate them prior to their introduction to the general profession in order to determine their hazards, applications, methods of administration and expected results.

Dr. Moyer's discussion was concerned with one aspect of his experience with antihypertensive therapy, i.e., the emergencies. Since there is a difference in the rationale for, and possibly results of the long-term treatment of chronic hypertension as opposed to the acute therapy of the crises, it may be well to discuss this subject for a moment.

Regarding the prolonged treatment of chronic hypertension with the newer therapies there are those who claim an inability to obtain the consistently good results from some of the antihypertensive agents which they were led to expect from reading the literature. Others state that decreasing the blood pressure may be an interesting clinical experiment, but that it has not been proven conclusively that the progress of vascular disease, which in the final analysis is responsible for pathology, has been halted or its tempo decreased since patients still succumb to, or are incapacitated by their strokes, "coronaries" and nephropathies in spite of their lower blood pressures. In some cases a sudden marked lowering especially in the elderly may precipitate irreversible cerebral or myocardial ischemia and injury. Some feel that in a number of patients mild to even moderate hypertension would be preferred to the various disturbing symptoms associated with the use of some of the presently available more potent drugs. Still others argue that there is a large group of benign "essential hypertensives" frequently seen in office practice who are asymptomatic, have no evidence of cardiac, renal or retinal damage, require no treatment except reassurance and possibly Rauwolfia preparations, and who probably should not even be informed of their blood pressure readings for fear of inducing symptomatic iatrogenic anxiety neurosis. A statement not infrequently quoted and applicable to this latter group is that "The blood pressure apparatus ranks next to the internal combustion engine in the list of inventions that have been harmful to the human race." Dr. Moyer, I am sure could present much evidence and muster many arguments in rebuttal, but these objections, problems and questions are raised not for the purpose of debate at this time and certainly not to deprecate the long-term treatment of chronic hypertension, but rather to indicate how different is the attitude toward and results of treatment of hypertensive emergencies.

Here a vascular accident, acute heart failure or eclampsia is imminent or has just occurred. The patient's life is frequently at stake and the indications are to immediately decrease the blood pressure which

has suddenly become elevated to extremely high levels from occasionally a normal, but generally a previously hypertensive level. The question of the relation of the level of hypertension to the degree of, or progression of arteriosclerosis is of no concern, nor are we attempting to secure some supposed future benefit from present treatment. If effective, the results of therapy are immediately evident and the relief of symptoms is generally directly correlated with the fall of the blood pressure. Results may be striking and relief may be rapid.

Most of us will recall our feeling of helplessness when confronted with these emergencies only 10 years ago. Management consisted of one or more of the following: venesection, lumbar puncture, hypertonic glucose or sucrose, aminophylin, magnesium sulfate orally, rectally and parenterally and sometimes intrathecally and narcotics and sedatives. In spite of this imposing array we were never confident or certain that we would successfully reduce the pressure. The situation is different today. We now have at hand not one, but several drugs which can do the job effectively, either alone or in combination. I sometimes wonder if more lives will not be saved and disabilities prevented by the proper use of parenteral antihypertensive drugs in these emergencies and in the malignant phase of hypertension than by the use of oral preparations for the continuous long-term treatment of every patient with elevated blood pressure.

All are agreed that this field is still in its infancy, and that pharmacologists will find newer and better drugs with less of the hazards, side effects, difficulties of administration and possibly even less expense to the patient. Dr. Moyer discussed mecamylamine, the newest antihypertensive agent. In the months to come there will undoubtedly be many more. Today's drugs may well be outmoded next year. For the present, for hypertensive emergencies it seems to me that each of us should be thoroughly familiar with the use of reserpine for the reasons discussed by Dr. Moyer, and one or more of the faster acting ganglionic blocking agents namely hexamethonium, mecamylamine or pentolinium when rapid reduction of pressure is required. Because of its emetic effect, the veratrum group of drugs will probably never be very popular. Occasionally as noted several drugs must be used in combination to secure the required effect. The possibility of pheochromocytoma or other chromaffin tumors in patients with sudden elevation of blood pressure must always be considered and in this instance Benadaine or Regitine is the drug of choice for both diagnosis and emergency therapy and surgery is the method of cure. Although some time was devoted to this disease in the discussion it should be noted that it is quite rare and that there is probably less than 1 to 1,000 chance that a hypertensive crisis is due to this rather than to hypertensive disease.

I enjoyed Dr. Moyer's presentation and again wish to express my admiration for his many contributions in this field.

Dr. Moyer (Closing). I want to thank Dr. Schnur for his kind remarks and I would agree 100 per cent that pheochromocytoma is not an important entity insofar as frequency is concerned. It is considerably more important when viewed from the pharmacodynamic aspect and relationship of these dynamics to essential hypertensive vascular disease. It is also of some importance to consider this entity even though it does not occur very frequently because the patient with this tumor will always turn up unexpectedly and can present a relatively embarrassing situation at the autopsy table.

It is essential to understand the pharmacodynamics of norepinephrine which is secreted by this tumor if one is to understand the treatment of essential hypertensive vascular disease. Norepinephrine is normally secreted by the post-ganglionic neuron of the sympathetic nervous system following stimulation. It is this substance which is responsible for the mediation of the neuron impulse from the sympathetic nervous system to the neuro-effector organ in the blood vessel. Therefore, when one considers it in this light, it is of increasing importance that we understand the pharmacodynamics of pheochromocytoma, norepinephrine, and their relationship to essential hypertensive vascular disease.

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Coxa Magna*

JOHN P. ADAMS, M.D.,† *Washington, D. C.*

The author describes two instances of an uncommon orthopedic condition encountered in childhood.

THE PATHOLOGIC STATE TERMED COXA MAGNA was first described as a clinical entity by Ferguson and Howorth,[1] the original report appearing in 1934. Since that date only one subsequent report has been found, published in 1935 by the same authors.[2]

Two children with disease of the hip joint that seem to fall into the entity termed coxa magna form the basis for this review.

Case Reports

Case 1. L. M., a 9 year old colored boy, was first examined in December 1949.

The history revealed the complaint of pain in the right hip and leg of one month's duration. He had been limping since the onset of the pain. The pain occasionally awakened him from a sound sleep; there was increased pain with activity. No history of chills or fever was given.

Family history was noncontributory.

Past History. The only serious infection was bacillary dysentery in 1943.

Physical Examination. Temperature, pulse and respiration were normal.

Orthopedic Examination. The child walked with a slight limp and with the right knee flexed. All passive hip motion was painful. The leg lengths were equal. No contractures were present. Motion was as follows: abduction 40°; flexion 95°; external rotation 20°; internal rotation 0°. Small, nontender lymph nodes were palpable in the inguinal area and atrophy of three-quarters of an inch was present in the right thigh.

The initial clinical impressions were tuberculosis, or a slipping of the femoral capital epiphysis. The child was admitted to the hospital in February, 1950, and placed in Buck's traction. Routine laboratory work was within normal limits. The tuberculin test was negative.

Roentgenograms, February 20, 1950 (Fig. 1A). Several areas of decreased density were present in the acetabulum and metaphysis. The joint space was of normal width.

The child was discharged on crutches.

October 14, 1953. The child had not returned to the clinic for one year. Pain had returned. There was limitation of flexion and internal rotation.

November 20, 1953. The patient was readmitted to the hospital. Laboratory examinations: Kahn, negative; phosphorus 4.8 and 9.8 mg.; alkaline phosphatase 5.0 units; acid phosphatase 5.2 units; hematocrit 46 per cent; WBC and urinalysis were normal.

Roentgenograms (Fig. 1B). During the period between the first admission and the second there was progressive enlargement of the femoral head and neck. Accompanying this enlargement of the head and neck were alterations in the trabecular pattern and increased density of the neck. The joint space remained normal.

December 10, 1953. A biopsy of the hip was done. Grossly, the synovium was described as thickened and a 1.0 by 9.5 cm. area of cartilage was detached from the articular cartilage. Cultures were negative for the tubercle bacillus, other bacteria, and fungi.

The patient was discharged on crutches.

January 17, 1954. The patient was asymptomatic, but motion remained limited.

October 29, 1954. There were no complaints. There was a half inch shortening of the right lower ex-

FIG. 1, A

These films depict the progressive changes in case 1. (A) Feb. 22, 1950.

*Read before the Section on Orthopedic and Traumatic Surgery, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

†From the Department of Surgery (Orthopedics), The George Washington University School of Medicine, Washington, D. C.

FIG. 1, B

(B) Feb. 6, 1952.

tremity; flexion was 70°, internal rotation 25°, external rotation 45° with the hip flexed.

Roentgenograms. There has been slight increase in the size of the head and neck. The trabeculae are more uniform in size. The density of the head is normal.

September 26, 1955. The patient was asymptomatic, and walked without a limp. There was slight limitation of rotation. The affected leg was 1 cm. shorter.

Roentgenograms (Fig. 1C). The joint space is of normal width. The capital epiphysis is regular in outline. (Fig. 1D.)

Case 2. R. B., an 8 year old white boy, gave a history on June 29, 1953, of pain in his right leg and limping of three months' duration. The child denied any injury. The limp progressed in severity during the day, and pain awakened the child at night. There was no history of chills, fever or malaise, nor weight loss.

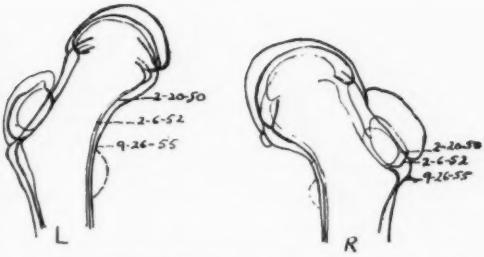
Physical Examination. The temperature, pulse, respiration and general examination were within normal range.

Orthopedic Examination. The child walked with a definite hip limp. There was a half inch atrophy of

FIG. 1, C

(C) Sept. 26, 1955.

FIG. 1, D



(D) This represents superimposed tracings of x-rays of the involved and uninvolved hips. By comparison of the tracings, the exact site of the abnormality in growth can be easily seen.

the right thigh. Motion of the hip was markedly limited in rotation. The hip flexed to 90°, abducted to 20°; a 40° flexion contracture was present.

Roentgenograms (Fig. 2A). A generalized density about the right hip with some cystic changes about the epiphyseal line was seen.

The boy was hospitalized at The George Washington University Hospital. Complete laboratory studies were carried out and all were normal. Tuberculin test was negative.

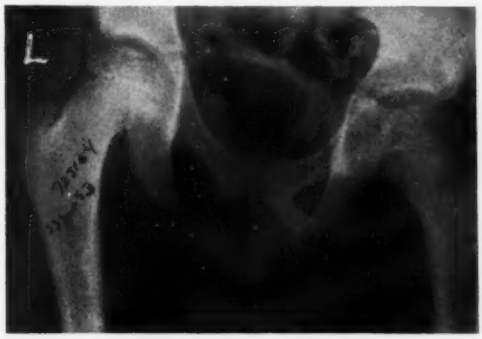
Initial impressions were: (1) Tuberculosis?; (2) Neoplasm?; (3) Early coxa plana?

Course. In the absence of any systemic reaction and a negative tuberculin reaction, tuberculosis seemed unlikely. The child was placed on crutches and used a sling to support the affected extremity. He continued to have limitation of motion and pain.

Roentgenograms (Fig. 2B). There was progressive enlargement of the head and neck with marked alteration in the trabecular pattern and increased density in the basilar neck area. The epiphyseal plate was normal except for decreased density. On September 22, 1953, an area of decreased density had developed in the neck of the femur.

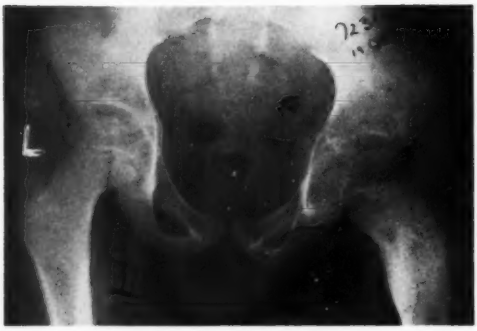
In January, 1954, the child was admitted to the hospital and a biopsy of the neck and trochanter was done. Following operation the symptoms subsided and

FIG. 2, A



Serial roentgenograms in case 2. (A) June 23, 1953.

FIG. 2, B



(B) Dec. 19, 1953.

the range of motion slowly improved.

On August 15, 1955, the child was completely asymptomatic. He walked without a limp and had normal range of hip motion. The leg lengths were equal, but 2 cm. of thigh atrophy was still present. Roentgenograms showed restoration of the trabecular pattern to one of near normalcy. The joint was of normal width. The capital epiphysis was normal. There was generalized enlargement of the head and neck (Figs. 2C and 2D).

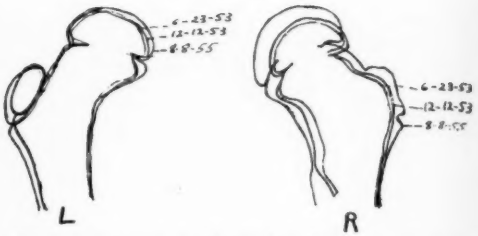
Discussion

Ferguson and Howorth in their original description of this syndrome stated that the syndrome of coxa magna was due to ischemia secondary to subacute arthritis. They felt that the impairment was not sufficiently great, or the part not sufficiently vulnerable, to result in coxa plana or slipping of the epiphysis. They also pointed out that occasionally in mild cases of coxa plana, or epiphyseal slipping, there is elongation of the neck of the femur with a broad, well-formed head and neck. These authors stated that in their opinion the

FIG. 2, C

(C) Aug. 8, 1955.

FIG. 2, D



(D) This represents superimposed tracings of x-rays of the involved and uninvolved hips. By comparison of the tracings, the exact site of the abnormality in growth can be easily seen.

overgrowth of the head and neck occurs with lesions of the neck or tissues adjacent to the hip. The overdevelopment may continue after the adjacent lesion has been cured.

In the second publication by the same authors 13 cases of coxa magna were described. The physical findings were similar to those of coxa plana. Pain was the presenting symptom in all cases. Many of the children gave a history of a preceding respiratory infection. The roentgenograms showed broadening of the head and neck in all. The joint space was wider than normal in 4, normal in 7 and thin in 2. All cases had exploratory operations. Pathologically, there was thickening of the soft tissues about the neck, synovial membrane and capsule. Histologically, there was congestion with a mononuclear infiltration. The vessels were thick walled. The bone and cartilage were described as normal. All cultures were negative.

The cases presented in this report also show pathologic evidence of synovitis and osteitis.

Conclusions

1. Two cases of hip joint disease in children have been presented which seem to fall within the abnormality termed coxa magna by Ferguson and Howorth.
2. The etiology of the disease is obscure.
3. Treatment is empirical.

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2. Ferguson, A. B., and Howorth, M. B., Jr.: Coxa Magna, J.A.M.A. 104:808, 1935.

Discussion (Abstract)

Dr. Kenneth R. Duff, Houston, Tex. I wish to compliment Dr. Adams on his very splendid presentation and the slides which he has used to demonstrate these

two cases. He has reviewed two cases of hip joint disease in children which have presented some of the clinical, pathologic and roentgenologic features of Legg-Perthes' disease; yet which recovered after a long period with enlargement of the head and neck of the femur. This syndrome has been termed, as he has said, coxa magna.

These cases have had, to my thinking, several points in common, namely, the age at the time of their onset, the one was eight and the other nine, the early complaint of pain in the leg, the atrophy of the thigh, the night pains, and the limp on the affected side.

The laboratory data was helpful only in the exclusion of certain types of infection. The biopsy material which was taken from the region of the hip joint showed thickening and perivascular cuffing, as his slides demonstrate.

The x-ray examination showed early cystic changes adjacent to the epiphyseal plate, and delayed enlargement of both the head and the neck. In each instance, the normal trabecular pattern was restored by the time the symptoms had subsided.

To me it is of interest that the capital epiphysis was spared in both cases and showed none of the characteristic changes that we see in Legg-Perthes' disease.

The essayist has referred to the work of Ferguson and Howorth. These authors recognized and later reported cases showing that the syndrome called coxa magna could arise in a number of ways and was characterized by enlargement of the head and the neck. They pointed out that the symptoms in these cases improved with rest and did poorly when immobilized, stretched or manipulated. I think Dr. Adams' cases illustrate these points.

I have not seen a case which I thought demonstrated these particular clinical and x-ray findings. I am sure that we will keep these two cases which Dr. Adams has reported to us in mind, recognizing their relationship to early Legg-Perthes' disease and certainly the very early stages of slipping epiphysis.

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CASE REPORT

Intrahepatic Obstructive Jaundice During Prolonged Administration of Propylthiouracil*

JOHN C. ALLEY, M.D., and JOHN M. RUMBALL, M.D., *Coral Gables, Fla.*

INTRAHEPATIC OBSTRUCTIVE JAUNDICE is becoming a more frequent problem in the differential diagnosis of jaundice. The cause of this increasing incidence is due at least in part to the increased use of certain therapeutic agents such as methyl testosterone, chlorpromazine, methimazole, thiouracil and its derivatives, and paraminosalicylic acid. In developing a history from the jaundice patient one must inquire into the use of these compounds mentioned in addition to the usual hepatotoxic agents.

Methyl testosterone[1] and chlorpromazine[2] are the most common offenders in the production of intrahepatic obstructive jaundice. Thiouracil and its derivatives have been found to cause such toxic reactions as skin eruptions, fever, and leukopenia.[3] In 1945, Gargill and Lesses[4] reported two patients who developed jaundice during the third week of treatment with thiouracil. In one instance the patient was operated upon for obstructive jaundice. At operation no obstruction to the extrahepatic biliary tract was found. However, biopsy of the liver revealed bile stasis and distended small bile ducts. No biopsy was done on the second patient but the symptoms and laboratory data suggested obstructive type of jaundice. In 1955, Shipp[5] reported the occurrence of jaundice in a patient who was being treated with methimazole (Tapazole).

The following is a report of a patient who developed jaundice following eight years of treatment with propylthiouracil.

*From the Medical Service, Veterans Administration Hospital, Coral Gables, Fla.

Case Report

F. M., a 58 year old white man, was admitted to this Veterans Administration Hospital on March 2, 1955, with complaints of pruritis and increasing jaundice. He had been in his usual state of health until the onset of the above complaints, three weeks before entering the hospital. The patient also acknowledged vague discomfort in the right upper quadrant of the abdomen as well as increased belching and slight nausea immediately after meals. The urine was noted to be dark colored and the stools light colored.

Inquiry as to habits, use of drugs, etc., failed to reveal a history of alcoholism, recent injections, transfusions of blood or plasma, or previous episodes of jaundice.

Fourteen years before the onset of this illness he noted fatigue and palpitations. Hyperthyroidism was diagnosed and treatment consisted of subtotal thyroidectomy. He was well for six years when again he noted excessive fatigue and palpitations. His physician then prescribed propylthiouracil in dosage of 50 mg. twice a day. The patient took this medication for eight years without supervision. On one occasion he discontinued propylthiouracil for a few days, but because he seemed to feel better while taking the medication he returned to the usual dosage. He denied taking any other drugs.

Physical examination revealed numerous excoriations scattered over the trunk and extremities. He was intensely jaundiced. All the vital signs were normal and the blood pressure was 140/74. There was an operative scar over the thyroid area of the neck. The eyes were slightly prominent but not definitely exophthalmic nor were any of the eye signs of exophthalmic goiter present. The resting and sleeping pulse rate ranged between 72 and 80 per minute. The liver was palpable and nontender about 4 cm. below the costal margin in the midclavicular line. The rest of the physical examination was entirely normal.

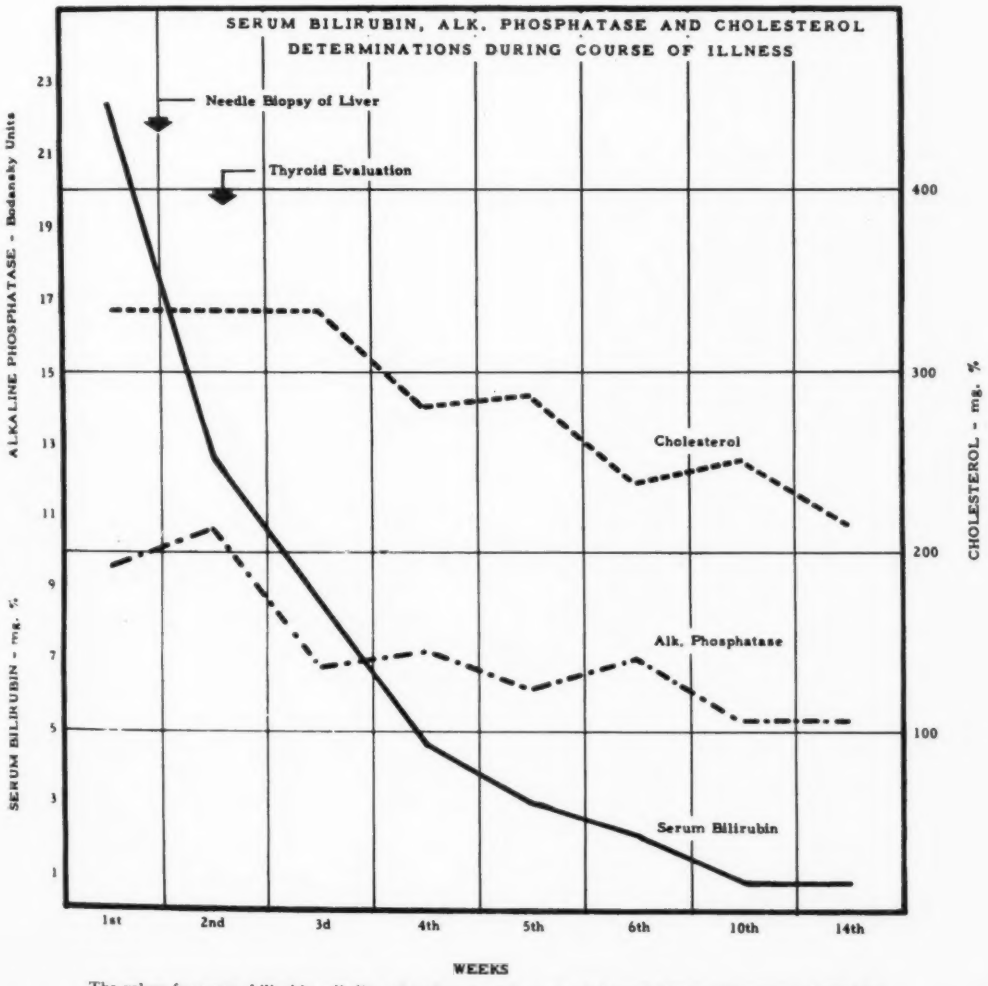
Laboratory data. Urinalysis, hemoglobin, hematocrit, white blood count, sedimentation rate, serum

amylase, and serum lipase were all considered normal. The following battery of so-called "liver function tests" were performed at weekly intervals: serum bilirubin, alkaline phosphatase, serum cholesterol and cholesterol esters, cholesterol cephalin flocculation, thymol turbidity, serum proteins with albumin-globulin ratio and, when nonicteric the Bromsulphalein excretion test. Standard technics for these procedures were used. Abnormal values are plotted in figure 1 (serum bilirubin, alkaline phosphatase and cholesterol). The remaining liver function tests were all normal. The Bromsulphalein excretion, determined when the serum bilirubin was 0.95 mg. per 100 cc., was 4.1 per cent (5 mg./Kg. read at 45 minutes). A needle biopsy of the liver was done at the end of the first week in the hospital (Fig. 2).

Hospital course and comments. Unknown to us this patient continued to take propylthiouracil daily for the first three days after admission. The medication was stopped and from then on he received no drug therapy. As is noted in figure 1 the serum bilirubin gradually declined to normal levels in six weeks. At the end of this period a cholecystogram revealed normal concentration of the dye without evidence of calculi. After the patient had received no propylthiouracil for a week there was a rapid and noticeable diminution of the icterus. The serum bilirubin dropped from 22.4 mg. to 12.6 mg. per 100 cc. Surgical intervention for obstructive jaundice was under consideration but because of this rapid drop it seemed advisable to wait, particularly since we suspected the cause of the jaundice to be due to the use of propylthiouracil.

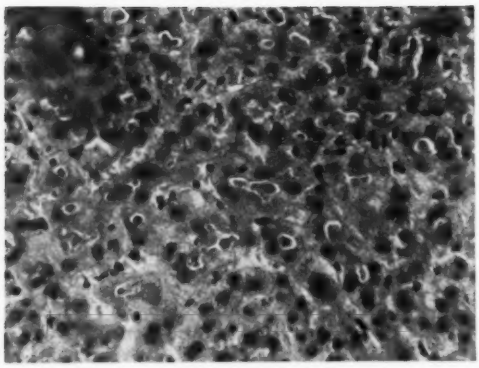
This patient was restless, somewhat overactive, and

FIG. 1



The values for serum bilirubin, alkaline phosphatase, and serum cholesterol during the course of jaundice.

FIG. 2



Needle biopsy of liver shows essentially normal architecture. Numerous bile casts are seen in the central areas and also in the periphery of the lobules (appear black in photomicrographs).

a sequential history was hard to obtain. In other words, he showed many of the manifestations of an individual with increased thyroid activity. The resting and sleeping pulse rates were always normal. The basal metabolic rate was plus 9, the protein-bound iodine was 6.3 gamma per 100 cc. and the radioactive I^{131} uptake was 58 per cent. These tests were all done during the second week of hospitalization at which time he was moderately jaundiced. One month later the I^{131} uptake was 37 per cent at which time the serum bilirubin was 3.0 mg. per 100 cc. Two months later the I^{131} uptake was 4 per cent at which time the serum bilirubin was normal.

Discussion

Most probably the increased I^{131} uptake was due to the effects of the propylthiouracil; yet the liver injury may have influenced the results. Mueller[6] and associates found an increased radioactive iodine uptake in 50 per cent of patients with Laennec's cirrhosis. The final radioactive iodine uptake studies were very low, indicating a hypothyroid state. No treatment was given since clinically there was no direct evidence of hypothyroidism, and the scintograms revealed a normal amount of thyroid tissue.

The mechanism of the production of bile stasis, causing intrahepatic obstructive jaundice, is not understood. This type of jaundice does occur when there is no history of any medication that might be implicated. Theories have been suggested that the mechanism is a state of hypersensitivity, involving the small bile ducts only; also, that there is some change in the bile constituents. Regardless of the mechanism it is difficult to understand how this patient could ingest this drug daily for eight years before the occurrence of jaundice. It is therefore possible that there is no cause and effect in this instance; on the other hand it appears beyond our knowledge at this time to prove it was not the cause.

Summary

1. A patient with intrahepatic obstructive jaundice is presented, who had been taking 100 mg. of propylthiouracil daily for eight years without previous untoward reaction.

2. It is believed that propylthiouracil was the cause of bile stasis yet there is no proof. The reports of this complication are few.

3. The increased incidence of this type of obstructive jaundice makes it more important than ever that a careful investigation be carried out before surgery is advised.

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Practical Aspects of Formation and Prevention of Urinary Tract Calculus:

A Review of 200 Successive Cases*

L. DOUGLAS ATHERTON, M.D., and
LYTLE ATHERTON, M.D.,† *Louisville, Ky.*

The problem of the cause of calculi in the upper urinary tract remains unanswered. However, by attention to adequate study and management recurrence can be prevented in many patients.

WE ALL THINK WE KNOW SOMETHING about the crystalloid aspect of calculus formation, and most of us are eagerly awaiting more information on the colloid factors involved. However, in the average community with average facilities, the application of our knowledge has certain difficulties. As we elaborate on a small series of cases that any one of you could easily duplicate, we will discuss these.

Before we get into this, some doctors may ask how important is it to investigate stone formers for possible causes of their trouble. In this series of 200 consecutive cases, 96 or almost 50 per cent had either multiple stones or gave a history of the repeated passage of stones. Because of the stones with or without complicating or causative infection, fifteen and one-half kidneys were removed. Two people died a kidney death despite all reasonable precautions, and at least two others are certain to do the same. Obviously the time to apply therapy in these people who have multiple stones is when the first stone appears, not after a kidney has gone to pieces. Most of us will agree, therefore, that something besides solution of the immediate problem of pain and fever is distinctly worthwhile.

The second question might be: Granted that there is a need for investigation directed at prevention, how effectively can we prevent future stones?

It is doubtful that anyone can say just how effective a strenuous application of all possible preventive measures can be. It would involve extremely accurate follow-up of a large number of cases over several decades. As things stand this is practically an impossibility. In a small proportion of the stone problems, however, there is no doubt but that further trouble has been avoided by diligent treatment. And it is only logical that correction of any one recognized factor should decrease the chances of stone formation, whether it entirely prevents further stones or not. This stands without proof.

To review briefly the generally accepted means of investigating stone problems you are directed to table 1.

History

History, especially of the diet, is an obvious first step. How many of us pay much attention to this factor? Of the 200 cases examined in this series, as aware as we think we are of the material set out in this paper, we could find written evidence that only 142 patients were asked about their diet. Some were probably asked and the point not recorded (especially if the data all appeared on a hospital form, the item itself being negative, and the

TABLE 1

PATHS FOR INVESTIGATION IN URINARY STONE FORMERS

History, especially of diet
Renal function (clearances, Cl, CO_2, blood pH, concentration tests, N.P.N.)
Rule out obstruction not due to stones
Identify and locate infection
Urinary pH chart
Stone analysis or identification
Rule in or out hypercalciuria and causes

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†From the Department of Urology, University of Louisville School of Medicine, Louisville, Ky.

doctor "pushed" for time on that particular day); some were problems of obvious infection, or of some other striking cause, and diet was not even considered.

How important is diet in the etiology of stone? In the case of calcium stones one can hardly belittle the fact that a quart of milk contains approximately 1,130 mg. of calcium, that about two-thirds of ingested calcium in most adults is excreted in the urine, that a diet containing 200 to 300 mg. calcium per day is sufficient to keep the average adult in positive calcium balance, that positive calcium balance can be maintained (barring, of course, the placental drain during the last two months of pregnancy, the period of lactation, and a few disease states) on an average diet without the addition of milk or cheese, and that pathologic conditions causing hypercalciuria are known to be associated with a high incidence of urinary tract calcium stones.

Three or four persons in this series, all of them presenting serious stone problems, were in the habit of drinking 2 to 3 quarts of milk daily. One patient lived on a farm and he rarely drank anything else. The others who drank from a pint to a quart of milk daily (the amount of cheese consumed is more difficult to estimate by history) may or may not have had their stones on this basis. Certainly, many non-stone formers appear to handle a relatively high calcium diet without urinary tract precipitation. But given a calcium stone former, it seems reasonable to reduce the concentration of dietary calcium in the urine if there is a history of moderate calcium intake.

From interviews with many patients, it seems easier to dilute urinary calcium by restricting dietary calcium than by increasing urinary output. Both, of course, are desirable. It is simply harder to drink anything when one is not thirsty than to substitute another beverage when one is thirsty.

With regard to the uric acid stone formers, we have yet to interview one of these patients who admitted eating enough high purine foods to make restriction seem anything but foolish. This has been true for the most part of high oxalate containing foods in oxalate stone formers.

Renal Abnormalities

Renal function studies are of most value in rare instances when one has to decide between primary and secondary hyperparathyroidism, or when there is a question of renal tubular acidosis. In either case one must establish nondietary hypercalciuria before any substantial improvement in stone-forming tendency might be expected to follow therapy.

One could hardly become a urologist without being very conscious of all types of *obstructions and anomalies of the urinary tract.* Infections often accompanying stasis, and the slowing of current seem to have definite implication in stone formation. One patient in these 200 appeared to have all her stone problems born in a ureterocele, and another in a calyceal diverticulum.

Infection needs some comment. It is almost a certainty that some infections, particularly those producing an alkaline urine, cause stones. Which came first is often impossible to establish. One woman had a known proteus infection in one kidney treated strenuously for four months by the most effective antibiotic by sensitivity tests. Despite this, she developed several large phosphate stones and lost her kidney. Science failed miserably in this instance, and brute force won out.

Of the 200 cases, 43 had infection identified. Of the 43, we were able to get rid of the organism without removing a kidney in 7.

In efforts to wipe out an infection after stones are removed one runs into the extremely practical problem of cost. One sometimes tries to balance the probability of creating a sterile urine against the expense involved in a reasonable trial with sensitivity-indicated fancy drugs. A reasonable trial is an arbitrary definition and may run into several months. In general, our experience in eradicating a long-standing pyelonephritis is rather unsatisfactory. It would be helpful if the drug houses had available more liberal provisions for such cases.

Urinary pH

The importance of *urinary pH,* of course, is related to the wide range of solubility of phosphates, uric acid and cystine.

We think it best to equip the patient with a vial of nitrazine paper and a pH color chart and instruct him to wet a strip at each voiding, recording the pH and time of day. He continues recording each voiding *while on*

his usual diet for about five days. In the case of calcium stones, one looks for a significant swing into the alkaline side. If, as some say, the nucleus of calcium oxalate stones is usually phosphate, then correcting the pH toward the acid side should be beneficial for all calcium stones except those containing cystine.

Exactly what constitutes a significant swing into the alkaline side by this test may call for an arbitrary definition. With an average American diet, we do not know what the average urinary pH chart would show other than that it is acid most of the time.

Albright and Bloomberg[1] once commented that calcium phosphate casts disappear from the urine at about a pH of 6.1. In interpreting pH charts, we have considered a pH of 6.0 and below a distinctly acid, and 6.5 and above as relatively alkaline. With this in mind, we can establish a workable acid: alkaline ratio out of the pH chart. In calcium stone formers with a 4:1 or less ratio, we consider it well worth trying to increase this.

This is attempted first by instituting an acid ash diet. We have a mimeographed diet sheet with foods listed under headings *Eat* and *Do Not Eat*, including most foods likely to be eaten and likely to influence the urinary pH. Stringent diets are not apt to be adhered to for very long unless the patient has a constant reminder of his illness. But this diet is not bad, and many comment that most of the foods therein are much to their liking anyway.

While on this diet the patient is instructed to keep another pH chart, and if the ratio is still less than 4:1, we add sodium acid phosphate in amounts up to 6 grams a day. Again he checks his urine pH to decide how much to take.

This failing, as it did in one patient, we have tried ammonium chloride. The latter drug in this particular person achieved the desired effect, but it also increased his basal urinary calcium output by about 70 mg. The relative acidosis caused by the ammonium chloride increased mobilization from bones, as happens in most types of acidosis.

As you will be quick to point out, infection makes the urinary pH charts unreliable and often unalterable. One lady in the series had a distinctly positive test (ratio decidedly less than 4:1) until her stone was extracted and infection overcome, and then it reverted to a negative picture (ratio considerably greater than 4:1) without diet or medication.

Whether the borderline positive charts have anything to do with calculus formation or not is certainly disputable. But the theoretical beneficial result of obtaining a negative chart should be acceptable to all.

In the case of uric acid stone formers, in the absence of infection, the chart will not show any markings above 6.0. This is a good way to rule out uric acid stones in a patient who indubitably had ureteral colic and in whom a stone was not visualized by x-ray and not recovered. If the chart swings up on the alkaline side and infection has been excluded, he cannot have had a uric acid stone.

Analysis of Stones

Stone analysis in some cases is helpful. Most of the time one knows by the x-ray or physical appearance of the stone what its composition is: calcium oxalate and/or phosphate, uric acid or cystine.

In laboratories and hospitals in the average town to which stones are only occasionally sent for analysis, the results are sometimes not clear. One laboratory reported to us that a stone was positive for phosphate, oxalate, and uric acid. Just how positive, which ingredient was predominant, and what the core consisted of was left to the imagination.

We now employ a scheme of analysis used at the Massachusetts General Hospital. The chemicals and a few simple tools were easy to acquire, and one of us did the analyses until some efficiency could be achieved and the process passed on to a technician. The difficulty is that the chemicals lose potency with time and need replenishing in relatively small amounts about every month. It takes about 10 minutes per stone, and even very small pieces can be investigated to some extent.

Hypercalciuria

A very important point of investigation in calcium stone formers is the ruling in or out of *nondietary hypercalciuria*. The causes of hypercalciuria usually agreed upon are listed in table 2.

For the most part they all evolve from

TABLE 2

CAUSES OF HYPERCALCIURIA

Excessive calcium intake
Suddenly induced prolonged recumbency
Renal tubular acidosis
Vitamin D excess
Idiopathic hypercalciuria
Hyperparathyroidism
Hyperthyroidism
Sarcoidosis
Progressing osteoporosis
Certain metastatic neoplasms to bone
Multiple myeloma
Paget's disease of bone

either too much calcium being absorbed from the intestine, or from some type of bone disease. One quickly establishes the former by inquiring about diet and vitamin intake. Establishing a nondietary hypercalciuria is a bit more formidable.

In a well-equipped large institution where the ordinary blood chemical determinations are done by graduates in college chemistry and everyone aims at accuracy, the results are one thing. In the average community where the doctor works in two or three hospitals and has relatively poor rapport with the laboratory chief who, because of limited budget, must hire less skilled and usually overworked personnel, the results are something else. The number of delicate laboratory tests a doctor must have done on his patient before he believes the result mounts up, and so does the cost to his patient. The thought of cost influencing the quality of care is distasteful to practically everyone, but that particular item plays a part in more ways than most of us care to admit. At any rate, in the average community one tries to make the most out of the simpler tests before resorting to a major laboratory undertaking.

The problem, again, is identification of nondietary hypercalciuria. It does not matter what blood chemical studies show in these calcium stone formers unless too much calcium is demonstrated in the urine. The Sulkowitch reagent and test is extremely simple, costs practically nothing, and everybody knows about it. Three precautions are advised in the use of the Sulkowitch test. (1) Learn to read it yourself; it takes only a minute of time. Anything interpreted in pluses and not in cold figures means less to everyone except to the one doing the interpreting. (2) Always note the specific gravity of the urine sample. We have never seen a 3-plus Sulkowitch in a urine with a gravity of 1.010, for example. Quick and definite 2-plus tests with a gravity of 1.015 to 1.020 are usually significant, as may be a 1-plus with a gravity of 1.010. The more positive the Sulkowitch test in relatively dilute urine, the more significance it has. (3) Make sure the patient is on a relatively low calcium diet when the urine is examined. For practical purposes this means exclusion of gross quantities of milk and cheese. This will rule out hypercalciuria in most of the stone patients.

If the Sulkowitch test is questionable or high, it is time to have a quantitative urine calcium determination done. We give our patients a mimeographed sheet instructing them in a strict low calcium diet which is followed for four days. On the last day a 24 hour urine specimen is collected and the calcium in this is quantitated. Results over 150 mg. we consider excessive and deserving of further study. The 24 hour urine calcium, blood calcium, phosphorus, and protein are then repeated until some conclusion is reached.

Obviously, in this phase of investigation a reliable laboratory is most important since minor deviations in accuracy will cloud the result. In some instances the laboratory will have to be verified by trial and error. Sometimes we are working in a hospital with dubious or unproven laboratory accuracy, and we simply try to complete this aspect of the problem after the patient recovers from his immediate situation and leaves the hospital. Confusing or contradictory laboratory reports are worse than none at all.

In the past few months we have used the phosphate reabsorption test as described by Kyle in an effort to more positively identify the patients with suggestive hyperparathyroidism. The test shows promise.

We are indebted to Dr. Robert Hendon of Louisville for his help in verifying and managing the parathyroid problems, and to Dr. George Sanders for his skill in removing the proved adenomas.

In cases of questionable hyperparathyroidism where one is faced with the possibility of a negative neck exploration, we think there is little harm in waiting a bit, repeating tests in a year or so. It is safe to assume that the

disease is slowly progressive and that its chemical trail will become more evident as time goes on.

Some of the interesting problems in hypercalciuria are illustrated in table 3. Other causes of hypercalciuria are usually more easily ascertained and often more difficult to correct.

Uricosuria

Uric acid stone formers should be considered separately. They need a permanent routine to maintain relative alkalinization of the urine, and the pH chart is invaluable in this situation. They take 25 per cent sodium and/or potassium citrate solution in sufficient quantity once daily to bring about a pH change to 7.5. The fairly accepted routine has been to maintain a constant alkaline urine by medication four times daily, but this is complicated for working people and more likely to be forgotten or abandoned. It seems reasonable to suppose that one strong alkaline swing per day will take care of small precipitations until they can be washed out. None of the seven such patients in this series has thus far formed more stones on one time a day alkalinization. If sodium or potassium is contraindicated, for some reason, in treating these patients, it may be possible to get equally good alkalinization with carbonic anhydrase inhibitor (Diamox).

Out of curiosity we measured the 24 hour uric acid urinary output in three cases. Two were normal, and the other put out only 800 mg. (normal being 500 to 700 mg. per 24 hours). The difficulty appears to be in the acid-making mechanism of the kidney, although uric acid determinations lack something to be desired, even if done precisely.

Results of Study

With the above as background, it may be of interest to recount our experience with 200

TABLE 3

INTERESTING PROBLEMS OF HYPERCALCIURIA

Case	*Urine Sulk.*	*24 hour Urine Ca*	*Ca (mg.)*	*Blood P (mg.)*	*Protein (Gm.)*	*P.R.T.*	*Conclusion*
C. H. S.	High	343 mg.* R 198 mg. R	11.5	2.9	R		Suggestive of mild hyperparathyroidism. Economic situation and relatively slight deviation from normal led us to defer investigation temporarily.
A. H.	High	559 mg.* R 255 mg. R 321 mg. R	10.0 10.0	3.9 4.4	7.1 R R		Idiopathic hypercalciuria. pH chart worth converting. Last urine Ca measured while on ammonium chloride.
H. T. M.		64 mg. R	12.0	3.3	UR		Blood work done first at time of hospitalization. Urine normal, even conceding some error.
Mrs. W. H.	High	239 mg. UR 80 mg. UR	11.6 11.8 9.9	3.1 3.2 3.3	7.7 UR UR UR		Last set of figures obtained after 6 months treatment for postmenopausal osteoporosis.
Mrs. B. H.	High	336 mg. R 338 mg. R	13.0 12.0	3.8 2.8	6.3 R R		Proven parathyroid adenoma.
Mrs. R. Z.	High		15.0 7.2	3.2 3.4	Q Q		No conclusion. Blood work done at different laboratories, both of unproven accuracy.
S. J.	High	174 mg. UR 96 mg. UR	11.0 11.0	2.7 2.8	7.2 UR UR		Negative neck exploration. Last urine is postoperative. Developed mild tetany from parathyroid devascularization. Also thyroid adenoma.
C. N.	High	378 mg. R 249 mg. R 193 mg. R 270 mg. R	13.0 12.5 12.0	2.8 3.1 3.0	7.1 R 7.1 R 6.8 R	Pos.	Probable hyperparathyroidism. Should be explored.
J. H. H.	High	242 mg. UR 186 mg. R	12.1 13.0 11.6	3.5 3.4 4.0	6.9 UR R	Neg.	Suggestive hyperparathyroidism. Negative phos. reabsorption test leaves us wondering.
Mrs. K. B.	High	72 mg. R					Urine volume 375 cc.! Denied error in collection.

*Not on strict low calcium diet.
R—Reliable laboratory.
UR—Usually reliable laboratory.
Q—Questionable or unproven laboratory.
P.R.T.—Phosphorus reabsorption test.
Sulk.—Sulkowitch test.

TABLE 4

FACTORS POSSIBLY INFLUENCING STONE FORMATION IN 200 CASES

Stones	Number		Infection Found			Hypercalciuria (Quantitative)			pH 4:1 or Less			High Calcium Intake		
	Single	Multiple	Single	Multiple	No. Investigated	Single	Multiple	No. Investigated	Single	Multiple	No. Investigated	Single	Multiple	No. Investigated
Unknown Composition	21	9	0	4	30	0	2	2	0	2	7	0	2	15
Calcium (Not analyzed)	51	45	9	12	89	3	9	24	3	7	24	7	9	64
Calcium Phosphate	13	27	5	8	36	0	9	16	1	8	18	1	10	32
Calcium Oxalate	17	9	2	2	26	1	4	6	2	1	9	4	1	23
Uric Acid	2	5	0	1	7	0	0	0	0	0	7	0	0	7
Cystine (Questionable)	0	1		0	1		0	0		0	0		0	1
	104	96	16	27	189	4	24	48	6	18	65	12	22	142
Total	200		43 of 189			28 of 48			24 of 65			34 of 142		

consecutive cases of urinary stone. We have tried to classify these cases in a way to give maximum information, as presented in tables 4 through 8. With a little advance information they may be reasonably intelligible.

On the basis of what we know of the composition of the stones, the cases are divided into six groups, and within the six, multiple or repeated stone formers are considered separately from those presenting an only occurrence of a single stone. The unknown group consists of patients with undoubted signs of ureteral colic and with confirmatory x-ray and urinary findings, but in whom the stone was not certainly visualized and not recovered. Some of these may have been of uric acid, although the probability is that most were very small calcium stones. A large group consists of those having calcium stones, by x-ray appearance, which were not analyzed for some reason or another. The other groups were analyzed and classified as predominantly phosphate, or oxalate. All the uric acid stones were pure ones. One small stone was produced by a patient with a negative family history and with no cystine crystals in the urine. We were surprised when our analyst reported that it was weakly positive for cystine.

TABLE 5

MISCELLANEOUS CAUSATIVE FACTORS IN 200 CASES OF STONE

Recumbency suddenly induced in young adult (Polio)	1
Recumbency and senile osteoporosis	3
Peptic ulcer with mandatory high Ca and alkali intake (not Burnett Syndrome)	3
Post-menopausal osteoporosis	1
Urinary tract anomalies	2
Questionable vitamin or nutritional deficiency	1
Questionable renal tubular disease	1
Total	12

TABLE 6

HYPERCALCIURIA

Stones	Blood Studies Done			Blood Studies Not Done
	Not Hyperparathyroidism	Suggestive Hyperparathyroidism	Proven Hyperparathyroidism	
Unknown Composition	1	0	0	1
Calcium single (Not analyzed)	2	1	0	0
Calcium multiple (Not analyzed)	4	5	2	0
CaPh single	0	0	0	0
CaPh multiple	4	3	1	2
CaOx single	0	0	0	1
CaOx multiple	4	0	0	0
Total	15	9	3	4

CaPh—Calcium phosphate
CaOx—Calcium oxalate

Table 4 lists factors possibly influencing stone formation, and with this the number of patients in whom the factor was inquired about or investigated. For several reasons, some good and some bad, not every factor was investigated in every patient. As may be seen, those with multiple stones got the most attention. The hypercalciurias include only those patients in whom quantitative 24 hour urines were done. The majority of the remaining patients had hypercalciuria excluded quite well by the Sulkowitch test.

Table 5 tells in another way the factors of stone formation in a few patients.

Table 6 breaks down the instances of hyper-

TABLE 7

PROBABILITY OF FINDING CAUSATIVE FACTOR(S)* IN 192 CALCIUM STONE FORMERS

Stones	*0 Factors Investigated* No. of Cases	*1 Factor Investigated* Found Positive	No. of Cases	*2 Factors Investigated* Found Positive	No. of Cases	*3 Factors Investigated* Found Positive	No. of Cases	*4 Factors Investigated* Found Positive	No. of Cases
Unknown Composition	2	1	10	2	12	3	4	2	2
Ca single (Not analyzed)	1	5	18	8	22	4	7	3	3
Ca multiple (Not analyzed)	3	4	12	4	9	8	9	12	12
CaPh single	0	2	5	3	5	0	1	2	2
CaPh multiple	0	0	2	4	6	7	8	11	11
CaOx single	0	0	2	4	10	2	3	1	2
CaOx multiple	0	0	1	1	3	1	2	3	3
Total	6	12	of 50	26	of 67	25	of 34	34	of 35
		24%		38.9%		73.5%		97.1%	

*Factors considered: high Ca diet, infection, nondietary hypercalciuria, and correctable urinary pH.
CaPh—Calcium phosphate
CaOx—Calcium oxalate

calciuria in relation to parathyroid disease. The majority of these, as nearly as we could tell, had idiopathic hypercalciuria.

Table 7 attempts to say that there is at least one potentially correctable stone-forming factor in almost every case of stone if all the factors are investigated.

Table 8 elaborates a bit more on the uric acid stone formers.

Table 9 summarizes preventive therapy. This is well-known information, but the point of this paper is to stimulate better application of what we already know.

TABLE 8

URIC ACID STONE FORMERS

Incidence (of 200 stone cases)	7 or 3.5%
Multiple or repeated stones	5 out of 7
Urinary pH charts	All consistently 6.0 and below
Infection	1 (probably postcystoscopy)
Obesity	3 out of 7
Elevated blood uric acid	1 of 3 tested
Blood dyscrasia	Not apparent in any
History suggestive of gout	4

TABLE 9

PREVENTIVE THERAPY

General Measures
High urinary output
Anti-infection management
Correction of obstructions or anomalies
Calcium Stones
Remedy hypercalciuria
Acidify urine
Reduce urinary phosphate
Uric Acid and Cystine Stones
Alkalinize urine

We emphasize high urinary output rather than high fluid intake because, after all, it is the urinary dilution factor that counts. We simply tell patients to put out at least two quarts of urine daily, to measure output occasionally on cold days and hot, and to drink enough water to accomplish this. We get the information in a lot of them when they bring in the 24 hour urine for quantitation; very few are over a 1,500 cc. volume.

The only other item in table 9 needing comment is the reduction of urinary phosphate. We have tried three patients on Basaljel. One of them has an ulcer whose stomach continually demands milk and alkali without consideration of its own kidneys. It is probably worth trying Basaljel in some of these patients who have almost irremediable stone problems, although it is doubtful if patients stick to it very long. One of our friends, a doctor extremely well-oriented in the stone problems, tried taking 400 cc. Basaljel daily to see how agreeable it actually was. He reported that his intestinal tract practically solidified and the ensuing misery forced him to end the experiment prematurely. Smaller amounts of the substance undoubtedly bind some phosphate and can probably be tolerated better. The use of stilbestrol on a long term basis usually has obvious disadvantages.

Summary

We have tried to indicate the importance of applying what we actually know about the formation and prevention of stones in the

urinary tract. We have pointed out problems in the practical application of this knowledge and have attempted a few solutions. A small series of 200 successive cases has been presented as illustrative material.

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Discussion (Abstract)

Dr. H. King Wade, Jr., Hot Springs, Ark. Dr. Atherton has presented a paper, which is of extreme practical interest to all of us as practicing urologists. He has given us a very fine discussion of a problem which, unfortunately, will continue to be a problem for many years to come. I make this statement because I do not believe we have all the answers to calculus formation. It is a happy situation that many of our researchers are vitally interested in this problem and are constantly at work on it. All of us sincerely hope the day will come when we will be able to more fully help the people who are chronic stone formers.

I was rather amazed at the extremely high percentage of patients in this series of cases (50 per cent), who had either multiple stones or gave a history of the repeated passage of stones. In reviewing the statements of many of the authorities on this subject, I find most of them have placed the figure at between 20 and 33 and one-third per cent. Of course, we realize that any series of cases so studied will show varied percentages.

We all recognize certain more or less fundamental procedures to carry out in an attempt to establish the cause or causes of recurrent stone formation. In my brief experience as a practicing urologist, it has consistently amazed me that I have come up with so few positive findings. I wonder if this has been the experience of many of you. Time and time again thorough studies of the urinary tract have failed to reveal obstructive phenomena. I place only one exception to this statement,—that is regarding recurrent urinary bladder calculi. In the great majority of these cases obstruction either in the form of prostatic hypertrophy or urethral stricture have played predominant roles, but I am consistently amazed at my failure to demonstrate upper urinary tract disease in the presence of so many cases of recurrent stones in the upper tract. I agree with Dr. Atherton that many of these patients do show chronic infection, but I have seen case after case in which the infection was overcome and in which the patients have formed more stones without obvious cause. Dr. Atherton's remarks concerning the various blood chemical studies were of interest to me since my findings concur with his. It has been extremely rare in my experience to demonstrate any marked elevations of the blood calcium, phosphorus or uric acid. Probably the Sulkowitch determination of the urinary calcium is a much more accurate indicator of what is going on. I do not believe that I have ever seen a blood chemistry report that in any way led me to suspect the presence of parathyroid adenomas. Variation in thyroid activity has not been too unusual and in the majority of my cases has been hypoactive in nature.

Again one of our greatest problems in attempting to establish programs to prevent recurrent calculi has been the patient himself. It has been our experience that while the patient was having his colic or recovering from his operation he was extremely anxious to do anything and everything to help prevent any further such personal disaster. But within a few weeks after recovery these good intentions seem to "fly out the window." The patients do not stay on the prescribed diets, they do not take the Basaljel and they do not report for follow-up laboratory and x-ray studies. Pain makes a believer of them for a short while, but their belief does not seem to last very long.

In conclusion, I feel that we have two major problems confronting us in the prevention of the recurrence of urinary calculi. The first is completing our knowledge of the causes and control of urinary calculi, and the second is obtaining and maintaining the cooperation of the individual patient.

Dr. Ray M. Babbitt, Huntington, W. Va. The Drs. Atherton have given us a broad review of their experience in renal calculus disease and brought out rather clearly that there is still a missing link. We agree that it is often impossible to carry out all the laboratory procedures indicated because of lack of facilities or cost to the patient. However, there are certain accepted predisposing factors in stone formation that must be corrected if possible. Infection must be eliminated, obstructions corrected, the presence of parathyroid tumors ruled out and, after careful study, the urine kept acid or alkaline as the case requires. The fact that stone formation can take place without any of these factors being present makes the problem more futile. I, personally, think that infection in most cases is secondary. We have two cases of stone formers who changed the character of their stones as the urine was either acidified or made alkaline.

Whether the missing link is metabolic, chemical, endocrine dysfunction or a combination of these plus other factors is still to be discovered. Fortunately, this unknown factor often rights itself which is well illustrated by the following case.

A man, age 36, reported six years ago with large bilateral staghorn calculi, with a proteus infection on one side and a mixed infection on the other and with definite renal damage. An operation had been done on each kidney with prompt recurrence. His parathyroid glands were explored at one of the large clinics with negative findings, and he was advised to have no further surgery and that the prognosis was very poor. He refused to accept this decision and insisted that we at least try. Over a period of four years we did five operations, three on the left and two on the right; the last ones being semi-permanent nephrostomies which were irrigated by his wife four times daily for over four months. All the antibiotics and their combinations were used. There was no further stone formation and the tubes were removed. Up to this time their 18 years of married life had been childless. As he stopped forming stones his wife became pregnant. The child is now 2 years old and he has remained stone free.

One patient formed uric stones over a period of three years. Eight years ago the stones ceased to form although the blood uric level is still just as high as before.

Abdominal Pregnancy*

DOUGLAS M. HAYNES, M.D., *Louisville, Ky.*, and
G. C. NABORS, M.D.,† *Dallas, Tex.*

The diagnosis of this condition can only be improved by an increased "index of suspicion" in a woman with evidences of pregnancy and complaints of abdominal pain. The management of the situation has led to controversy.

SINCE ABDOMINAL PREGNANCY IS A RARE CONDITION, no one individual can expect to attain a large experience in its management. It is useful, therefore, to undertake periodic critical review of the accumulated published experience of others. This paper summarizes recent articles on the subject and reports a series of six previously unpublished protocols from a teaching service.

Patient Protocols

In the decade 1944 to 1954, seven women with abdominal pregnancies presented themselves at Parkland Hospital. One of these patients has been previously reported;[1] the other six (Table 1) are summarized below.

Case 1. L. J., a 30 year old primigravida, was first seen on March 5, 1947, complaining of intermittent vaginal bleeding for several months. Her last menstrual period began on July 15, 1946, and there had been intermittent irregular bleeding for the subsequent two months, associated with lower abdominal pain. A physician did a dilatation and curettage, but no improvement followed. In October the patient noticed a small mass which protruded from the vagina; this mass could be replaced at first, but not later on. The patient first felt fetal movement in late October.

On admission, a fetus was felt in an undetermined attitude and position. The hypertrophied cervix protruded from the introitus. The fundus was displaced inferiorly by a cystic mass; on a plain film of the abdomen, this mass was seen to contain a fetal skeleton. The tentative diagnosis of abdominal pregnancy was confirmed when the administration of one minim of pituitrin produced contraction in the prolapsed uterus, but not in the mass which contained the fetus.

At operation, the amniotic sac was encountered just beneath the parietal peritoneum. A normal living child weighing 2,402 grams was extracted, and the umbilical cord was ligated as close to the placental surface as possible. The placenta had become implanted in the vesicouterine space, extending laterally to both iliac gutters and upward to the level of the xiphisternum, and excluded from view all the abdominal viscera; it was not molested. The patient went home improved on the twenty-first postoperative day, but she promptly developed severe diarrhea. Three days later she had slight left flank pain, but she did not return until 10 days later when she presented the clinical signs of bilateral pyelonephritis.

Pyelography showed a hydroureter on the left, and a right hydronephrosis. A left nephrostomy was done. Thirteen days later, a large tender mass in the left lower quadrant was incised, and copious purulent fecal-smelling material was drained from it; subsequently a fecal fistula formed at this point of drainage. Placental debris appeared in the drainage, and a series of hemorrhages, varying in quantity from 50 to 250 cc., ensued at irregular intervals. In spite of intensive supportive treatment, the patient gradually became cachectic, and on June 7, 1947, she expired suddenly after a final hemorrhage of about 250 cc. At autopsy, necrotic placental tissue was found throughout the abdomen in approximately the locations described at the original laparotomy. There was secondary diffuse peritonitis, and a fistulous connection had been formed between a loop of ileum and the anterior abdominal wall.

Case 2. V. H., a 32 year old gravida II para I, complained on October 26, 1946 of a sudden severe abdominal pain of one hour's duration. Her last menstrual period had begun on September 22, and there had been some daily bleeding up to the time of admission; her last normal menstrual period had been in August. Three weeks prior to admission, the patient had an episode of sudden cramping right lower quadrant pain, diagnosed in the emergency room as being due to pelvic inflammation. The symptoms subsided upon routine conservative treatment, but on the evening of October 25 she had a similar episode of pain which ultimately spread over the entire abdomen, and was associated with progressive abdominal distention.

On admission the temperature was 99°, pulse 100, BP 110/70. The patient appeared restless and apprehensive. There was generalized abdominal tenderness, worse in the right lower quadrant and periumbilical area, and rebound tenderness most marked on the right. The cervix was displaced toward the left; a small amount of bloody mucus was present in the external os. The normal sized uterus was exquisitely tender on motion.

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†From the Departments of Obstetrics and Gynecology of Parkland Hospital and the University of Texas Southwestern Medical School, Dallas, Tex.

Under anesthesia, a semisolid mass was felt extending two-fifths of the distance to the umbilicus. Blood-tinged serous fluid was aspirated from the cul-de-sac. A hemoglobin determination at this time showed a drop of three grams from that recorded on admission. The clinical diagnosis was twisted ovarian cyst with intracystic hemorrhage. At operation, a thin-walled sac filled the abdomen and pelvis, and adhered to the bladder anteriorly. Profuse hemorrhage had occurred from an area of attachment of the sac to the posterior uterine surface. A 9 cm. fetus and a handful of clots were removed from the abdomen. Temporary hemostasis was obtained by placing packs against the bleeding area. Eventually, about one-third of the placenta was removed.

The patient had no further hemorrhage, and made an uncomplicated recovery. She was discharged in good condition on November 12, 1946, and has remained well since.

Case 3. F. E. R., a 27 year old primigravida, was admitted to Parkland Hospital on November 6, 1948 complaining of severe periumbilical pain and rebound tenderness throughout the abdomen. An abdominal mass was palpated in continuity with the cervix. The clinical impression was intraperitoneal hemorrhage secondary to abdominal pregnancy or ruptured cyst.

At operation, there was a hemoperitoneum of 2,500 cc. An ovisac containing an 18 cm. fetus was removed intact. The placenta was attached to omentum, posterolateral pelvic wall, sigmoid colon and cul-de-sac peritoneum. Bleeding was brisk and the patient rapidly went into shock; blood transfusion and hemostasis by packing ultimately brought about improvement in her condition. The placenta was left in situ. The patient made a good postoperative recovery.

Case 4. L. F., a 30 year old primigravida, was first seen on December 1, 1948. Her last menstrual period began on July 3, 1948. The patient had recently noted morning nausea, urinary frequency, and enlargement and tenderness of the breasts. On October 5, there was a small amount of vaginal bleeding for two days. On September 11, she described a "normal period" lasting three days. It was decided to follow her in the outclinic.

On December 14, the cervix was displaced retrosymphysially, and the uterus could not be outlined. A moderately tender left-sided mass filled the cul-de-sac. The clinical impression was that of a left tubo-ovarian abscess, and colpotomy was recommended.

On December 16, a large amount of old blood was aspirated from the cul-de-sac mass. When the abdomen was opened immediately thereafter, a massive hemoperitoneum was encountered. The uterus was displaced anteriorly and to the left by a large right-sided adnexal mass containing a small, partially extruded fetus of five months' gestation. There was brisk bleeding from the placenta, which was implanted on cul-de-sac peritoneum, posterior broad ligament and anterior rectal wall. Rapid hysterectomy was required to produce partial control of the bleeding; this had to be supplemented by mechanical pressure.

The postoperative course was surprisingly uncomplicated, and complete recovery had taken place when she was last seen on June 10, 1949.

Case 5. G. B. B., a 35 year old gravida III para I, whose expected date of delivery was November 22, 1949, was first seen on July 27, 1949. Two days before admission, she had noted intermittent "pulling pains" in the lower abdomen. Physical examination showed signs of pregnancy and a large, spherical, tender, fixed mass extending to the umbilicus on the right. The temperature was 102.4°; the blood pressure, 128/70.

Symptoms persisted, and on August 2, 1949, the abdomen was opened with a preoperative diagnosis of infected myoma with pregnancy. There were adhesions of the bowel to a tumor mass the size of a large grapefruit arising close to the right of the uterus. The large bowel and cecum were adherent to the posterior aspect of the mass. During the course of the separatory dissection, a small amount of pus oozed from the center of the mass, and a 20 cm. fetus was delivered. The right tube and ovary could not be seen, and undoubtedly formed an integral part of the mass, which was the ovisac. The latter was shelled out of its implantation in the right broad ligament, and the uterus was removed. During the course of the procedure, the right ureter was cut within 2 cm. of the bladder; it was reimplanted. The postoperative diagnosis was intraligamentous abdominal pregnancy. The nonviable fetus showed a left talipes varus and right talipes calcaneovarus. The patient continued to do well postoperatively, and was discharged in good condition.

Case 6. P. S., a 25 year old primigravida, was first seen on February 12, 1951, complaining of lower abdominal pain, intermittently present for one and a half months, but much more severe for ten hours. The last normal menstrual period had begun on November 25, 1950. Since December 26 the patient had vomited at least once daily. On the morning of admission she had a sudden attack of severe lower abdominal pain. On admission there was voluntary rigidity of both rectus muscles. The cervix was bluish

TABLE 1

CLINICAL DATA IN SIX CASES

Patient	*Age*	*Gestation at Operation*	*Preop. Diagnosis*	*Fetal Fate*	*Maternal Fate*	*Placenta*
L.J.	30	Term	Abdominal pregnancy	Survived	Died	Not disturbed
V.H.	32	12 wks.	Twisted cyst	Nonviable	Recovered	1/3 removed
F.E.R.	27	20 wks.	Abdominal pregnancy or ovarian cyst	Nonviable	Recovered	Not disturbed
L.F.	30	20 wks.	Tubo-ovarian abscess	Nonviable	Recovered	Not disturbed
G.B.B.	35	24 wks.	Infected myoma	Nonviable	Recovered	Not disturbed
P.S.	25	Term	Pelvic infection and pregnancy	Dead	Recovered	Marsupialized

and softened. The uterus was slightly enlarged. The tentative diagnosis was acute intraperitoneal pelvic inflammation coexisting with pregnancy, and conservative therapy was undertaken. By February 19, the patient had been afebrile for three days, and was ambulatory and relatively asymptomatic; she was allowed to go home.

Forty-eight hours later, she noted the sudden onset of intermittent supraumbilical pain followed by vomiting of a greenish fluid. On examination there was abdominal tenderness involving the entire lower abdomen, but no rigidity. An indistinct right-sided mass arose from the pelvis. The softened uterus was enlarged to about twice normal size. Conservative therapy was recommended pending fluctuation in the abscess. By March 28, however, the mass had apparently receded, and the afebrile, asymptomatic patient again left the hospital.

Seven days later there was recurrence of sharp lower abdominal pain described by the patient as "a little like labor pains," and associated with blood-stained mucoid vaginal discharge. Examination showed bilateral adnexal tenderness, and exquisite pain on motion of the cervix. She was observed in the hospital with diminution of symptoms and remained relatively afebrile from April 15 to May 9; on the latter day, her temperature rose to 102°, and she had slight lower abdominal pain. The symptoms continued intermittently, though the patient's general condition seemed improved.

On June 6, 1951, pelvic examination seemed to point to intrauterine pregnancy, and the previously palpated mass was less distinct. A plain film of the abdomen showed fetal bones compatible with a five and a half months' gestation; the bones were thought to be inside the uterus. A soft tissue mass was felt extending for 5 inches cephalad from the most superior portion of the fetus. The roentgen picture was suggestive of ovarian cyst, hydrosalpinx or mesenteric lipoma. On June 20, the fetal heart was heard in the right upper quadrant, and counted at 132 beats per minute, and the fundus rose to three fingerbreadths above the umbilicus.

The patient was kept in the hospital because of recurrent intermittent episodes of nausea, vomiting, cramping, fever, and lower abdominal tenderness. On September 24, an unsuccessful attempt was made to rupture the membranes, and two days later a second attempt was also unsuccessful. The uterus was then probed, the fundus being encountered at 4 inches. Tissue from the uterus showed decidual reaction.

At operation a large cystic mass was found filling the entire lower abdomen. When exploration was attempted severe hemorrhage occurred. A pack was held against the bleeding area and an opening was made into the amniotic sac. A dead, partly macerated, approximately term-sized fetus was delivered, and the umbilical cord was ligated close to the placenta. The omentum across the amniotic sac was ligated in as many places as possible, and a five yard roll placed in the abdominal cavity against the placental site in the right lower quadrant. The placenta had become implanted on the bladder, uterus, right posterior aspect of broad ligament, sigmoid colon, ileum and transverse colon. Marsupialization was accomplished by suturing the opening in the amniotic sac to the peritoneum at the superior part of the abdominal incision. Two abdominal packs were left extruding through the middle portion of the partially closed incision. Twenty-five hundred cubic centimeters of blood were given during and immediately following the operation.

The immediate postoperative course was surprisingly uneventful. Spontaneous foul-smelling drainage occurred from the abdominal wound, and there were frequent temperature elevations to 102°, but otherwise improvement was remarkable. The patient was discharged improved on November 5, 1951.

On December 3, 1951, she returned, and over a period of several hours the retained placenta was spontaneously extruded through the anterior abdominal wall defect as the result of rhythmical uterine contractions.

On June 4, 1952, the subumbilical incisional scar was approximately 2.5 cm. thick, and overlay a defect in the fascia of the anterior abdominal wall through which intra-abdominal viscera could be felt protruding when the patient coughed and strained. No masses were palpable. On June 16, 1952, abdominal hysterectomy and umbilical herniorrhaphy were done. Numerous old adhesions were found involving the omentum, small bowel and genitalia and especially the right tube, ovary and appendix. The patient was discharged in good condition on June 23, 1952, and has remained well since.

Discussion

The principal considerations in any discussion of abdominal pregnancy are: preoperative diagnosis, fetal salvage, maternal mortality, optimum time for operation, and management of the placenta. These features are best studied on the basis of accumulated published case reports. Others[2, 3] have collected and extensively discussed cases reported prior to 1944. A survey, admittedly incomplete, of articles published since 1944 was made in connection with the present report, and is summarized in table 2. The 40 patients with ovarian pregnancy are included for the sake of completeness, though the present discussion is concerned only with clinical problems of the remaining 149 patients.

TABLE 2

DURATION OF GESTATION IN 189 CASES

	Reported Cases 1945-1954	*This Series*
Ovarian pregnancy	40	0
Other abdominal pregnancy (143 cases)		
Less than 24 weeks	42	4
24 to 36 weeks	15	0
36 weeks or more	86	2
Total	183	6

Diagnosis. Table 3 summarizes the preoperative diagnoses of 189 women with abdominal pregnancy culled from the literature. It illustrates the difficulties inherent in the diagnosis, as do the additional case reports which have been presented. A high index of suspicion remains the most important diagnostic tool for recognition of abdominal pregnancy, so protean in its manifestations. It is well to keep the diagnosis in mind when the following features are present, whether singly or in combination: history of bleeding, pain, or other untoward incident six weeks after the beginning of a menstrual period, with subsequent temporary quiescence; recurrent episodes of intraperitoneal infection in the presence of a demonstrable pregnancy; palpation of fetal parts closely under the anterior abdominal wall, high in the abdomen and in abnormal presentation; displacement of the uneffaced cervix, usually anteriorly; and absence of a uterine shadow about the fetus on a plain film of the abdomen. Culdocentesis and exploratory colpotomy, which have been used with increasing frequency as aids to the diagnosis of early ectopic pregnancy, are of limited helpfulness in abdominal pregnancy. In fact, published reports do not suggest that the accuracy of preoperative diagnosis has increased appreciably during the past ten years.

Fetal Salvage. Table 4 summarizes published data on the fate of 149 fetuses delivered from patients with relatively advanced abdominal pregnancies. Diagnostic difficulties result in the preponderance of cases not recognized until the pregnancy has reached 36 weeks' gestation or more. It is noteworthy that in this group of advanced abdominal pregnancies, there is a fetal salvage of 52.2 per cent. Although few obstetricians would advise long-term temporization when the diagnosis of abdominal pregnancy is made early in gestation, these data suggest that there may be a limited place for short periods of delay in the interest of the fetus in cases diagnosed shortly before the thirty-sixth week of gestation, provided there are no untoward maternal signs or symptoms. In actual practice, the latter is only occasionally true.

TABLE 3

PREOPERATIVE DIAGNOSIS IN 189 CASES

Diagnosis	*183 Reported Cases 1944-54*	*Per Cent*	*This Series (6 Cases)*	*Per Cent*
Abdominal Pregnancy	51	27.9	2	33.3
Other or not stated	132	72.1	4	66.7

TABLE 4

FETAL SURVIVAL IN 149 CASES

Length of Gestation (Weeks)	*Total Cases Reviewed*	*Number of Living Infants*	*Per Cent*
Less than 24	46	0	0.0
24 to 36	15	2	13.3
36 or more	88	46	52.2

Maternal Mortality. There were 19 maternal deaths in the 189 cases summarized here, an over-all incidence of 10 per cent. However, only three of these reported fatalities occurred in women treated since 1944. Of these three women, only our patient reported above (L. J.) died of complications related directly to the abdominal pregnancy, the other two succumbing to tetanus[4] and respiratory infection[5] respectively. It is, of course, unjustifiable to maintain that a drastic reduction in maternal death from abdominal pregnancy is documented by these data. Fatal cases may go unreported, and no claim is made that the literature has been reviewed with anything approaching completeness. At the same time it is surely justifiable to suppose that the widespread use of blood transfusion and antibiotics in the period covered, as well as advances in the understanding of problems of fluid and electrolyte balance, will have exerted a significant effect on a disease the principal complications of which are hemorrhage, infection and their sequelae.

Optimum Time for Operation. There is no unanimity on the question of when operation should be performed on the patient diagnosed as having an abdominal pregnancy, but not presenting any specific indication for immediate intervention. It is often stated that operation should be done as soon as the diagnosis has been made, the argument being that the delay necessary to obtain a viable child is not justified in the face of the danger to the mother from potential hemorrhage and infection, and the high fetal mortality attendant on this type of pregnancy. On the other hand, other writers maintain that the available data are insufficient to determine with finality whether or not an abdominal pregnancy should be terminated before the thirty-sixth week in the interests of the

mother, but that in the absence of acute signs and symptoms there is no specific contraindication to allowing the pregnancy to continue to the stage of viability. In the series reviewed here, there were six instances of congenital fetal anomaly, a smaller proportion than that previously reported; however, the data on this point are scarcely conclusive.

Management of the Abdominally Implanted Placenta. Hemorrhage from the implantation site when removal of the placenta is attempted may constitute a formidable problem which is a justly feared complication of abdominal pregnancy. Since definitive ligature is not possible, hemostasis has to be attempted by unsatisfactory indirect means, such as mechanical pressure by abdominal packs. In those cases in which extensive peritoneal implantation of the placenta has taken place, it is probably advisable to tie off the umbilical cord as close as possible to the fetal surface of the placenta, and to avoid further disturbance of the implantation site. Since the beginning of the antibiotic era, physicians have been better able to control the resulting infection than was formerly possible, though the peritonitis, abscess and fistula formation which often follow such management of the ectopically implanted placenta must be considered as being the lesser of two serious evils.

Summary

1. Protocols are presented of six patients with abdominal pregnancy treated at Parkland Hospital during the years 1944 to 1954.

2. Clinical problems of abdominal pregnancy are discussed in the light of these cases and of 149 other cases reported in the literature during the same period.

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Discussion (Abstract)

Dr. W. P. Devereux, Dallas, Tex. At Baylor-Florence Nightingale Hospital, Dallas, during an eight year period, ending in 1953, there were 38,000 deliveries, with four abdominal pregnancies, an incidence of 1 in 9,200. Of these four cases, two were delivered at operation of living babies. One showed multiple anomalies and expired after 35 minutes. The other was a normal healthy infant, whose mother four years later was delivered vaginally of another normal child. In each of the other two cases a dead fetus was removed, one being markedly macerated. The other was contained in a thick-walled sac, surrounded by fluid, was soft and pliable even though it was 11 months past full term. This patient had been admitted to the hospital when three weeks past term for induction of labor because of a dead fetus, abdominal pregnancy not having been suspected. Since medical induction failed she was discharged to return one week later. Instead, she disappeared to return 10 months later, stating that she had gone to California to have the baby, but since she had never had it, decided to come back. She said she had menstruated regularly for six months and felt fine, but had a "lump in her stomach" which she would like to have removed. Operation was done 20 months after conception.

Disposition of the placenta in these four cases was as follows: two were removed, being attached almost entirely to the adnexa, the blood supply thus being available for ligation; two were left in place, one requiring subsequent drainage of abscess, and eventual removal of the adnexa on that side; the other patient was completely lost to follow-up despite efforts to locate her.

To illustrate how easily the diagnosis of early abdominal pregnancy can be missed, as Dr. Haynes and Dr. Nabors have pointed out, we may cite what happened in the total of 10 cases, 6 from Parkland and 4 from Baylor-Nightingale: 9 of the 10 had had one or more episodes of abdominal pain and vaginal bleeding in the first trimester; 6 of the 10 had been examined in the first trimester during an acute episode of pain, the diagnosis of extrauterine pregnancy not having been made, although it had been suspected at the time in two, the usual diagnosis was pelvic inflammatory disease; 3 of these 6 had been admitted to a hospital and observed, one for a whole month, another admitted on three occasions, still undiagnosed; and 2 of the 10 had had attempts at induction of labor.

I would like to emphasize again that the placenta should not be removed unless it is attached in such a location that its blood supply is available for ligation, even though subsequent operation may be necessary.

Dr. John Weed, New Orleans, La. There are two points I would like to mention. One is that diagnosis of abdominal pregnancy is often made when the patient at term does not appear to be ready to deliver. Thus the diagnosis was made in one of the patients mentioned by Dr. Haynes in which induction was attempted. We have had two such instances in which our resident staff has used a very simple means of confirming the diagnosis of abdominal pregnancy, by the cautious use of lipidol oil introduced into the uterine cavity.

We have very beautiful pictures showing the uterine cavity and fallopian tubes. No complications have arisen.

The other point I would like to make is this,—when the diagnosis of abdominal pregnancy is considered prior to the seventh month, and it is rarely made at that time, usually some intra-abdominal condition such as the intraperitoneal hemorrhage has led to the suspicion of abdominal pregnancy. Under those circumstances it has been our policy at the Charity Hospital in New Orleans to explore these individuals because temporizing is fraught with danger.

I can recall one such patient who was admitted with abdominal pain and tenderness and the diagnosis of intra-abdominal bleeding with abdominal pregnancy was entertained. The symptoms subsided and we felt that she could probably go on for an additional three or four weeks with care and observation in the hospital, but only to find that within a few more days, a more extensive intra-abdominal crisis approached and interruption was necessary.

For that reason, it has been our policy that once the diagnosis of abdominal pregnancy is made, regardless of the period of gestation, interruption is necessary.

Dr. Buford Word, Birmingham, Ala. I rise to confirm what Dr. Haynes so aptly stated in his paper, that is, the growth of a human life outside the uterus is hazardous. During a similar ten year period covered in Dr. Haynes' paper there were, at the University Hospital in Birmingham, Alabama, 391 extra-uterine pregnancies. Of these, nine were abdominal pregnancies which had survived early rupture and advanced to the seventh month or more of gestation. Abdominal pregnancies represent 2 to 3 per cent of all extra-uterine pregnancies. This is well stated in a monograph by Parry published in 1876. He collected 500 of the first reported cases of extra-uterine pregnancy in the world literature and found that in 149 early tubal ruptures there were 145 fatalities. Only four patients in 149 survived the initial crisis to harbor a fetus which might or might not have also survived.

At the present there is no comparison to Parry's research because immediate surgical treatment is nearly always instituted at the time of initial rupture, and Parry's statistics were compiled in the days when surgical treatment of this disease was not practiced.

It is a relief to know that Dr. Haynes and Dr. Weed did not diagnose all of their cases preoperatively. I shall discuss two of the nine University Hospital patients in whom the lesions were misdiagnosed.

One patient was treated alternately on the gynecologic service for pelvic inflammatory diseases and on the surgical service for intestinal obstruction from the time of the initial rupture at approximately eight weeks gestation to about the seventh month. She was in and out of the hospital four times during this period. In spite of antibiotic therapy for pelvic inflammatory disease and Miller-Abbott tube for relief of her intestinal obstruction, the fetus grew surreptitiously to seven months gestation. X-ray pictures of this patient's abdomen were made, but because of her obesity no shadow of a fetus was noted. Finally, the patient returned to the hospital in the middle of the night with symptoms and signs of intestinal obstruction. She did have a large epigastric hernia which, although present on previous admissions had not been thought to be the cause of her obstructive symptoms.

The resident on duty said, "It must be that hernia, let's fix it anyway." The patient was taken to the operating room, the hernial sac dissected free and excised and then, before closing, an exploration of the peritoneal cavity was begun. It was at this time the baby kicked the surgeon's exploring hand and it first became known the patient had an abdominal pregnancy.

In addition to the high maternal mortality in abdominal pregnancy there is an even higher fetal mortality and of the infants who do survive approximately 50 per cent are either deformed or mentally deficient. The mental deficiency is due to an impaired fetal blood supply.

On April 10, 1946, a colored patient who had been followed in the obstetrical clinic was admitted to the hospital, at term, in early labor and was known to have a mass in the pelvis which was thought to be a uterine fibroid. The patient labored unsatisfactorily for a period of eight hours. It was decided the fibroid was blocking the pelvic outlet and a cesarean section was indicated. She was taken to the operating room and this human life was removed from a sac in the abdominal cavity. The sac was thought to be the uterus. The baby weighed four pounds. The operator began to sew up the "uterus." It was thin and friable and for that reason Pitocin was injected to make it contract and become thick. The "uterus" did not respond to Pitocin stimulation and at this time an exploration of the pelvic structures was begun. A portion of the fresh placenta was torn loose which initiated uncontrollable hemorrhage and resulted in the death of the mother six hours later, despite all counter measures for combating blood loss shock.

Of the nine abdominal pregnancies this is the only infant who survived and his mother was the only maternal fatality. Her death was due to uncontrollable hemorrhage precipitated at the operating table, without knowing the placenta was implanted outside of the uterus until a portion of it had been pried loose.

This child is now 9 years old and is mentally deficient. His vocabulary is limited to one or two syllable words and he does not go to school.

Although abdominal pregnancy is rare, the best sign or symptom of which I know in diagnosing this lesion, early or late, is a constant awareness of the possibility of this disease when a woman says "My stomach hurts."

Radical Surgery, Electively, and After Radiation Therapy in the Treatment of Cancer of the Uterine Cervix*

J. KEITH CROMER, M.D., and MARGARET McCABE, M.D.,†
Washington, D. C.

In a search for better results in the treatment of cancer of the cervix the surgical approach and irradiation inevitably come up for comparison. The authors have evaluated their results in the hope of casting some light on the subject.

SURGERY AT THE PRESENT TIME is in the ascendency in the treatment of cancer of the uterine cervix, largely because of the poor over-all cure rate (reported as 40 per cent) obtained by radiation therapy.[1] Since, by inference, 60 per cent of the patients treated by radiation fail to obtain a cure, the trend away from radiation toward surgery is understandable.

There is an intense desire on the part of the surgically minded worker in the cancer field to improve the results obtained by radiation therapy. The radical hysterectomy of Meigs,[2] the transabdominal lymphadenectomy of Taussig,[3] the extraperitoneal lymphadenectomy of Nathanson,[4] and the evisceration procedures of Brunschwig[5] lend mute testimony to this effort.

That surgery has a place in the treatment of the early lesion (Stage I and Stage II, League of Nations Classification) has been amply demonstrated. Likewise, Brunschwig[6] has shown that ultraradical surgery as a "last ditch" procedure has something to offer the patient with advanced cancer who no longer has a chance for cure by any other form of treatment.

Except for its recent application in the treatment of the patient with uncontrolled or recurrent disease, surgery after radiation has never been accepted as ideal, largely because of the technical difficulties encountered and the untoward complications which follow this combined form of therapy. Other attempts at solving this problem have been efforts to determine beforehand, or early in the course of therapy, those cases which are not sufficiently sensitive to irradiation therapy to respond favorably to treatment. Such cases are surgical from the outset provided they can be accurately defined.

Despite these acknowledged disadvantages, the combination of radiation and surgery in the treatment of cancer of the cervix remains intriguing because it offers the hope of combining the good features of both methods of treatment, either of which used alone leaves much to be desired. The study reported here was undertaken to test this concept. The method for achieving this end is the presentation, for comparison, of results obtained in the treatment of two similar groups of patients, one treated by elective surgery and the other treated by radiation and surgery. Additional data included in this report are the number and nature of the major complications encountered, the frequency of regional lymph node metastasis for both series of patients, the incidence of residual cervical disease in the radiated and surgically treated group and the number of associated pelvic abnormalities in both series and their role in determining the end results.

Material

This series of 86 patients includes cases from the George Washington University Cancer Clinic, the George Washington University Hospital, and the senior author's personal

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†From the Department of Obstetrics and Gynecology, George Washington University Medical School, Washington, D. C.

Research Fellow, George Washington University Cancer Clinic, Washington, D. C.

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practice, and covers a period from January 1947 to August 1953. The patients were selected without regard to their general physical condition, age, race, or nutritional status. Except in two instances patients with demonstrable rectal involvement were excluded from the series. The diagnosis was made by biopsy in all cases.

Eighty-three patients had epidermoid carcinoma and three had adenocarinoma of the uterine cervix. The stage of the disease was recorded according to the League of Nations Classification. The age range in this series was from 22 to 69, with an average of 45 years. The median age was between 45 and 49 years.

Method

Eighty-six cases of similar patient material with cancer of the cervix were treated consecutively and, for the most part, in one institution,—46 by elective surgery and 40 by operation after radiation. The results are presented for comparison. Five patients in each group who received identical treatment at another institution are included in this study. The 46 patients in the first group (those treated by elective surgery) had received no previous specific treatment for their disease. Eight of this group received large doses of progesterone prior to definite surgery. The results of this study have been reported elsewhere[7] and will not be discussed at this time. In the first two years of the series only patients with Stage I and early Stage II lesions were considered suitable for surgery. After 1948, this method of selection was abandoned and the patients were treated surgically if the disease was considered amenable to surgical attack. The operative procedures employed were radical hysterectomy in 63 cases, anterior pelvic evisceration in 20, and total pelvic evisceration in one case.

The radical hysterectomy employed was the combination Wertheim hysterectomy and Taussig node dissection as described by Meigs.[2] Anterior pelvic evisceration includes the removal of the bladder and all or part of the vagina. Total pelvic evisceration combines the anterior variety with removal of the rectum. In the less formidable procedure, the rectum is preserved and the ureters transplanted into the rectosigmoid colon. In the complete procedure the ureters are implanted into the sigmoid colon above the end colostomy, thus establishing a wet colostomy. The technic used is similar to that previously described by Brunschwig.[6]

The 40 in the second group (those treated by radiation and surgery) had been treated by radium and/or x-ray irradiation. Thirteen patients in this group received intra-arterial Aureomycin and nitrogen mustard therapy concomitantly with x-ray therapy. The results of this study have been reported[8] and will not be dealt with at this time. Radium was used alone in two cases (both early Stage II lesions). External x-ray irradiation and intravaginal irradiation was the method in four cases. Seventeen patients received external x-ray irradiation and radium to the cervix. Eight patients received external irradiation, intravaginal x-ray irradiation and radium. Eight patients were treated with external irradiation alone, and one patient received intravaginal x-ray irradiation alone (Stage I lesion).

The methods of radiation therapy in this series have included 200 to 400 kilovolts of x-ray irradiation. In most cases, treatment consisted of 12,000 to 8,000 r, in air, given through external pelvic portals, followed in one week by radium application to the cervix.

For the most part the following external roentgen irradiation factors were: 200 K.V.; half-value layer, 1 mm. copper; target-skin distance 50 cm. Two external anterior and two external posterior fields were used. The fields were 8 by 10 cm., 8 by 15 cm., or 10 by 15 cm.

In five patients, the external irradiation factors were: 400 K.V.; half-value layer, 3 mm. copper; target-skin distance 75 cm. Two anterior and two posterior external fields each measuring 12 by 15 cm. were used.

The radium was applied through the use of a Campbell colpostat.

When ready for insertion the colpostat held 65 mg. of radium; 25 mg. in tandem in the cervical stem; 10 mg. in each of the cervical bars, and 10 mg. in each vaginal fornix. The filtration was equivalent to 1 mm. of platinum.

The dosage varied between 2,400 and 7,680 mg. hours given in either single or divided doses. Two patients in the series received radium alone to the cervix. Additional x-ray

TABLE 1

SUMMARY OF CLINICAL DATA ON TREATMENT OF CERVICAL CANCER BY RADICAL SURGERY, ELECTIVELY AND AFTER RADIATION THERAPY*

Year of Operation	Number of Patients	Stage of Disease	Diagnosis: Epidermoid	Diagnosis: Adenocarcinoma	Treatment: S	Treatment: RS	Positive Nodes: S	Positive Nodes: RS	Residual Disease: RS	Residual Disease and Nodes: RS	Interval between R and S in Months	Associated Pelvic Abnormalities: S	Associated Pelvic Abnormalities: RS	Alive and Well: S	Alive and Well: RS	Alive with Disease: S	Alive with Disease: RS	Post-operative Deaths: S	Post-operative Deaths: RS	Survival Period of Dead or Lost Patients in Months: S	Survival Period of Dead or Lost Patients in Months: RS
		I	4		3	1			1		12	1		2						22	66
1947	4	II																			
		III																			
		IV																			
		I	4	1	4	1					8	1		4	1						
1948	9	II	4		1	3			1	1	12;4;12							1		61	12;12
		III																			
		IV																			
		I	2		1	1			1		24	1	1	1	1						
1949	17	II	9		4	5	1		3	1	3;10;11;8;192	1			2	1		1	1	5;9	8;14
		III	2			2				1	8;24										61;51
		IV	4		3	1	2			1	9			1				2			36
		I	3		1	2				1	1;6		1	1	2						
1950	8	II	4		3	1	2			1	11			1		1				24	2
		III	1		1		1							1							
		IV																			
		I	4		4							3		3						24	
1951	15	II	5		3	2		1			47;3	2	2	1	2					36;14	
		III	4	1	1	4	1		1	2	2;4;8;6	1	2							9	2;8;24;24
		IV	1		1							1								12	
		I	5		4	1			1		2	2	1	4	1						
1952	15	II	6	1	4	3			2	1	3;14;8	2		3				1			16;10;2
		III	3		1	2				1	8;4	1		1	1						5
		IV																			
		I	4		4							1		3						8	
1953	18	II	10		3	7	2		3	3	6;4;6;10; 10;2;5	3	2	1	5					8(1 lost)	14;7
		III	3			3			2	1	11;6;6		1					2			1
		IV	1			1					6		1		1						
	86		83	3	46	40	9	1	15	14		20	11	27	16	2		4	4		
		I	26	1	21	6			3	1		9	3	18	5						
Total		II	38	1	18	21	5	1	9	7		8	4	6	9	2		2	2		
		III	13	1	3	11	2		3	5		2	3	2	1				2		
		IV	6		4	2	2			1		1	1	1	1			2			

*Key. R, for radiation; S, for surgery; RS, for radiation and surgery.

irradiation was given intravaginally through a vaginal cone in 13 cases. The transvaginal factors were: half-value layer, 2.0 mm. Al.; target-skin distance 21 cm.; cone size 3-3.5 cm. The dosage for this form of x-ray irradiation ranged from 5,000 to 8,000 r, with an average of 6,400 r.

During 1947-1948, only patients classed as Stages I and II, as indicated in table 1, were selected for definitive surgery after radiation therapy. These patients were selected largely by serial Papanicolaou smears.

After 1948, patients were selected for operation after radiation therapy by the same method used in the group treated by surgery electively. If upon pelvic examination the existing condition was considered open to surgical attack, the patients were hospitalized and definitive surgery performed.

As mentioned earlier in this paper, patients with demonstrable rectal involvement were excluded from the series (with two exceptions). For the most part, the patients in this series were operated upon as soon after completing their treatment as was considered feasible. The interval between radiation therapy and definitive surgery is summarized in table 1. To some extent, long intervals were due to economic reasons and the patients' resistance to hospitalization for operation. The longest interval, 16 years, between radiation and surgery occurred in one patient who had received intracavitary radium at a distant clinic, in 1933, for excessive bleeding. At the initial examination she was classed as Stage II and was treated by elective surgery. The interval of 47 months between radiation and surgery in one case was due to the fact that the patient failed to report to the clinic and was not available for operation.

Prior to operation, each patient had a general medical appraisal, including proctoscopic and cystoscopic examination and intravenous pyelography. In addition, when indicated, roentgen examination of the colon by barium enema and of the kidneys by retrograde pyelography was made. Blood transfusions were given when necessary to bring the blood count and plasma proteins to within normal limits. In the early years of this series, each patient received 3 grams of sulfasuxidine every four hours beginning one week prior to the scheduled surgical intervention. During 1953, this was discontinued and the patient received 500 mg. of Aureomycin orally three times a day for three days before operation. On the eve of the fourth preoperative day, 45 cc. of castor oil were given by mouth. For three days prior to operation, the diet was restricted to clear liquids, and daily cleansing enemas were given. At the time of operation, Sodium Pentothal was used for induction and was followed by gas-oxygen-ether to insure surgical relaxation.

Postoperatively, constant gastric aspiration was maintained for at least 48 hours. At least 400,000 units of penicillin were given daily for five days. Fluid balance was maintained. In those patients treated by partial pelvic evisceration constant rectal drainage was carried out for seven days. Patency of the tube was assured by gentle daily irrigations with tap water. For two or three days postoperatively nothing was given by mouth. Thereafter, fluids and diet were gradually increased as the patient's tolerance permitted. Activity and ambulation were encouraged as early as possible.

The surgical specimens were fixed in Bouin's solution and serial blocks were removed for histopathologic study. The lymph nodes were carefully identified, enumerated, fixed, and sectioned for microscopic study. The number of patients with positive lymph nodes and residual carcinoma is summarized in table 1.

End Results by Methods of Treatment, All Stages (1947-1953)

The end results for the entire series are summarized and presented in table 2. Of the 86 patients included in this entire series, which began in January, 1947, and continued until August, 1953, 42, or 49 per cent, are alive and well without evidence of disease at the present time (November 1954). The "present time" used in this paper and in this connection refers to the status of the patients as of November 1, 1954. Of the 46 patients in the series treated by elective surgery, 27, or 59 per cent, are alive and well at the present time. Two are alive with disease. Nine partial pelvic eviscerations were done in this group and of these, 3, or 33 per cent, are alive and well, one at 55 months, one at 62 months, and one at 23 months. Forty

TABLE 2

END RESULTS BY STAGES AND METHOD OF TREATMENT (1947-1953)*

Stage	Treatment S No.	Treatment RS No.	Alive and Well S No.	Alive and Well S %	Alive and Well RS No.	Alive and Well RS %	Alive with Disease S No.	Alive with Disease S %	Alive with Disease RS No.	Alive with Disease RS %
I	21	6	18	86	4	67				
II	18	21	6	33	9	43	2	11		
III	3	11	2	67	1	9				
IV	4	2	1	25	1	50				
Totals	46	40	27		15		2			

Per Cent Surviving without Disease
Surgical 59; Radiation and surgery 38

64 Radical hysterectomies: 36 survived. (2 living with disease)

19 Partial pelvic eviscerations: 5 living and well

1 Complete pelvic evisceration

1 No surgical specimen (Patient died on the operating table after skin incision from myocardial infarction)

1 Colostomy for radiation necrosis of rectum

*Key
S—surgical
RS—radiation and surgery

patients were treated by radiation and surgery and of this number 15, or 38 per cent, are alive and well at the present time. Ten partial pelvic eviscerations were done in this group, and of these one patient is alive and well at 21 months. One patient in this group who had a partial evisceration survived 61 months, one died at 21 months from a pulmonary involvement and one died from a heart attack at 10 months. None of this group of 10 is alive with disease. One complete evisceration was done in this group. The patient died one month later from disseminated disease.

Five of the 8 patients in the surgically treated group who received progesterone prior to operation are alive and well at the present time. Four of the 13 patients who received intra-arterial nitrogen mustard and Aureomycin concomitantly with x-ray irradiation are alive and well at the present time.

There were eight postoperative deaths, four for each method of treatment, in the entire series, or an over-all immediate surgical mortality rate of 9 per cent. The surgical mortality rate for the group treated by elective surgery was 9 per cent, and for the group treated by radiation and surgery, 10 per cent.

Three patients died from other known causes,—one from multiple myeloma, one from a "heart attack" and one from pulmonary embolism. Four died from unknown causes.

Four patients were lost to follow-up,—one immediately after discharge from the hospital, one at 9 months, one at 14 months, and one at 23 months after treatment, and for statistical purposes are considered to be dead.

Long-Term Results by Methods of Treatment, All Stages (1947-1949)

In table 3 are summarized the five-year results and status of the patients by stages for both methods of treatment for the years 1947, 1948 and 1949. During this period, 30 patients were treated, 16 by elective surgery and 14 by radiation and surgery. Nineteen patients, or 60 per cent, survived five years. One patient with Stage II disease and 2 patients classed as Stage III survived five years with disease. The remaining 16 are alive and well without evidence of disease at the present time.

It should be noted that 4 patients classed as Stage II were treated by partial pelvic evisceration during this period. Two patients revealed invasion of the bladder in the surgical specimen and should be classed as Stage IV. Of the remaining 2, one revealed radiation necrosis of the bladder and one revealed no invasion of the bladder. Likewise, 2 patients in Stage III revealed invasion of the bladder and belong in the Stage IV category. As stated earlier, the staging of the

TABLE 3

SUMMARY OF FIVE-YEAR RESULTS AND STATUS OF PATIENTS BY STAGES (1947-1949)*

Stage	Treatment S No.	Treatment RS No.	Alive and Well S No.	Alive and Well S %	Alive and Well RS No.	Alive and Well RS %	Alive with Disease S No.	Alive with Disease S %	Alive with Disease RS No.	Alive with Disease RS %
I	8	3	8	100	3	100				
II	5	8	2	40	2	25	1	20		
III		2							2	100
IV	3	1	1	33						
Totals	16	14	11		5		1		2	

Per Cent Surviving without Disease
Surgical 69; Radiation and surgery 36

20 Radical hysterectomies (1 with ligation of vena cava): 15 survived

9 Partial pelvic eviscerations (4 for Stage II lesions): 2 living and well

1 No surgical specimen (Patient died on the operating table after skin incision from myocardial infarction)

*Key
S—surgical
RS—radiation and surgery

cases treated by radiation and surgery and listed in table 1 represents the clinical impression obtained at the initial examination prior to beginning of treatment. This finding was frequently checked and concurred in by two independent examiners and represents a fairly accurate report on the status of the patients at the beginning of therapy.

Since in these 4 cases the disease may have progressed one or more stages between the time of irradiation and the time of surgery, it was not considered desirable to shift these patients to a more advanced stage on the basis of later findings, although such an adjusted listing might in some instances improve the survival percentage for the numerically lower stage. It should be pointed out, however, that such listing would not alter the over-all survival percentage of the series.

Positive Lymph Nodes

The number of patients having metastasis to lymph nodes, residual disease, and/or both are grouped according to stages and shown in table 1.

No positive lymph nodes were found in the 21 patients operated upon electively for Stage I disease. Of 18 patients with Stage II lesions, 5, or 28 per cent, revealed lymph node metastasis. The fate of these 5 patients is interesting. One died at 9 months with spinal and pulmonary metastasis; 2 died in uremia, one at 24 months and one at 8 months, and one died from recurrent disease at 48 months. The patient with pulmonary metastasis had had a partial evisceration and rightfully belongs in Stage IV since the surgical specimen revealed invasion of the urinary bladder. A review of her x-ray studies revealed that the lesion had been present at the time of the operation but had not been diagnosed. Two of the 3 patients classed as Stage III, or 67 per cent, had positive lymph nodes. One of these died from disseminated disease at 9 months, and one is alive and well at 48 months. Of the 4 patients classed as Stage IV, 2, or 50 per cent, had positive lymph nodes. Both of these patients are included in the postoperative deaths.

Of 40 patients in the irradiated and surgically treated group only one patient revealed positive lymph nodes without residual disease. This occurred in a patient with Stage II disease. She is alive and well at 36 months.

Residual Cervical Tumor

The number of patients with residual tumor in the cervix after x-ray irradiation are listed by stages in table 1. Two patients included in the Stage II group should be eliminated from the series. One of these received an unknown amount of intracavitary radium in 1933 while under treatment in a distant clinic. At the initial examination, in 1949, she was classed as Stage II and treated by radical hysterectomy. The surgical specimen revealed cervical cancer and 15 negative lymph nodes by actual count. She died 14 months later with disseminated disease. The other one to be excluded was a diabetic who received

external x-ray irradiation, transvaginal irradiation and radium from October 15, 1947 to December 17, 1947 and failed to report to the clinic. A radical hysterectomy was performed 47 months later for what was thought to be advanced disease. The surgical specimen revealed leiomyomata, chronic bilateral salpingitis, and a fibroma of the ovary. She is alive and well at the present time.

Of the remaining 38 patients 13, or 45 per cent, revealed residual tumor in the cervix. Three, or 50 per cent, with Stage I cancer had residual disease, and of these 2 are alive and well. One died at 66 months from multiple myeloma.

Of 19 patients with Stage II cancer 9, or 47 per cent, had residual tumor and of these 6 are well. Two have survived 5 years. Of 11 with Stage III cancer 3, or 27 per cent, had residual disease, and of these none are alive. One survived 61 months and one survived 24 months.

Residual Disease and Positive Nodes

Fourteen patients, or 35 per cent, revealed residual tumor in the cervix and involvement of the regional lymph nodes. Of 6 patients with Stage I cancer, one, or 17 per cent, revealed residual cervical tumor and lymph node metastasis. She is alive and well at 41 months. Of 21 patients with Stage II disease 7, or 33 per cent, revealed positive regional lymph nodes and residual cervical disease. Two of this group are alive and well.

Of 11 with Stage III disease 5, or 45 per cent, revealed residual cervical disease and regional lymph node involvement. None of this group is alive at the present time. One survived with disease for 35 months.

Of 2 patients classed as Stage IV one revealed residual disease and positive lymph nodes. She survived 36 months after a partial pelvic evisceration and died from some pulmonary involvement.

Complications by Method of Treatment, All Stages

The complications reported in this study and presented in table 4 are believed to be those directly attributable to the method of treatment in the two series of cases. The most common minor complication and the one most disturbing to the attending surgeon was the patient's postoperative inability to void. This complication occurred almost universally in the series following radical hysterectomy and, besides being troublesome to the physician, was costly to the patient. It is undoubtedly due to interruption in the nervous control of the bladder and frequently lasts for weeks before the patient is free of residual urine.

TABLE 4

NUMBERS OF COMPLICATIONS BY METHOD OF TREATMENT—ALL STAGES

	Surgery	*Radiation and Surgery*	*Total*
Ureteral obstruction with hydronephrosis and pyelonephritis	2	2	4
Hyperchloremic acidosis	2	2	4
Fistula:			
Rectovaginal		4	4
Vesicovaginal		1	1
Ureterovaginal		2	2
Intestinal obstruction		1	1
Miscellaneous			
Hemorrhage, shock and sepsis		1	1
Necrosis of rectum		1	1
Surgical elephantiasis		1	1

Ureteral obstruction with resultant hydronephrosis and pyelonephritis was present in 2 patients in each series and was responsible for postoperative death in all 4 cases.

The syndrome of hyperchloremic acidosis which was encountered twice in each series was unrecognized in one, and responsible for one postoperative death.

There were no instances of the development of fistula in the group treated by elective surgery.

In the irradiated and surgically treated group there was one instance of severe hemorrhage, shock, and sepsis, from which the patient failed to recover. Of this group, one patient required a colostomy for radiation necrosis of the rectum, and one patient developed surgical elephantiasis of the vulva and both lower extremities following a radical hysterectomy and a bilateral dissection of the groin. This patient ultimately died of disseminated disease.

Associated Pelvic Abnormalities

Associated pelvic abnormalities encountered in the series are listed by method of treatment in table 5.

The large number of negro patients, 42 for the entire series (20, or 43 per cent, for the

TABLE 5

ASSOCIATED ABNORMALITIES BY METHOD OF TREATMENT

Surgical	*Number of Cases*	*Radiation-Surgical*	*Number of Cases*
Fibroids	11	Fibroids	10
Endometriosis	8	Endometriosis	4
Chronic lymphadenitis	1	Bilateral salpingitis, ovarian fibroma and fibroids	1
Granuloma lymph nodes	1	Epidermoid carcinoma of cervix and adenocarcinoma of uterus	1
Leukoplakia vulvae	1	Tubo-ovarian abscess	1
Adenocarcinoma of cervix with epidermoid carcinoma in situ	1	Non-caseous tuberculoid granuloma of inguinal and pelvic lymph nodes	1
Brenner tumor and endometriosis	1	Leiomyosarcoma of the uterus, fibroids, endometriosis, chronic iliac lymphadenitis	1
Hyperplastic lymph nodes	1		

surgically treated group and 22, or 55 per cent, for the radiated and surgically treated group), undoubtedly accounts for the high incidence of fibroids in both groups and for the large number of inflammatory lesions in the latter group. The lower incidence of endometriosis in the radiated and surgically treated group is considered a radiation effect.

Discussion

The results obtained from this study and a perusal of the current literature support the statement that the present methods for treating cancer of the cervix, i.e., surgery and radiation therapy, are not the answer to the problem. Both methods have their advantages and limitations. Surgery has a limited field of usefulness in the treatment of the Stage I and early Stage II lesion but offers palliation on a par with or better than that obtained by radiation therapy in the patient with advanced disease.

The over-all five year results (59 per cent) for those treated by elective surgery in this series compare favorably with results obtained elsewhere.

Stage III lesions, i.e., those with fixation to one or both pelvic walls, offer by far the most difficult problem to deal with surgically. Stage IV lesions with involvement of the bladder, and without fixation, can be dealt with surgically with survival rates (33 per cent) as good as those accomplished by radiation therapy, as has been shown in this series.

Surgery after irradiation as a routine procedure is a hazardous undertaking as shown by the results obtained and the complications encountered in this series. However, many of the patients treated by this method, including many with residual disease (67 per cent for the series), were salvaged, and 38 per cent of this group have survived and are alive and well at the present time.

As is often the case, favorable results which appear in the literature are confined to those obtained in small selected series. Unfortunately cancer is not a respecter of persons and to combat it better methods for treating all types of patients are needed. Present methods of therapy do not fulfill this obligation. While the over-all results, 59 per cent, for the surgically treated group and 38 per cent for the radiated and surgically treated group obtained in this series leave much to be desired in the treatment of cervix cancer, they do seem to indicate that elective surgery for all stages is superior to the combination of radiation and surgery. The large number of complications and the number of fistulas which developed in the radiated and surgically treated group confirm the belief that surgery after irradiation is a hazardous undertaking and far from ideal. The poor showing for the Stage II lesions in the surgically treated group is partly explained as errors in the diagnosis of the stage. Many patients in this category were found to have advanced disease and in many instances invasion of the bladder at the time of surgery.

In this series the finding of 9 patients, or an incidence of 20 per cent, with lymph nodes positive for metastasis in the surgically treated group is in keeping with results reported by Pratt,[9] i.e., 24 patients with positive lymph nodes in 171 patients, or an incidence of 14 per cent. Likewise, the incidence of 37 per cent with positive nodes in the irradiated and surgically treated group is in accord with other reports. Pratt[9] found 25 in 122 patients, or an incidence of 20 per cent among patients irradiated prior to surgery. Cherry and associates[10] reported an incidence of 45 per cent of positive nodes in 213 patients with Stage

I and II disease treated by radium and surgery.

The finding of 29 patients (67 per cent) in the radiated and surgically treated group with residual disease is indeed ominous. Since 34 patients treated by this method were included in Stages II, III, and IV categories this finding is understandable.

Undoubtedly the errors in clinical diagnosis of stages were considerable, and many patients classed as Stage II actually belonged in the advanced categories.

In this study it was the rule that when any uncertainty existed regarding the stage, the patient was placed in the prognostically more favorable category. It is reasonable to believe that the presence of residual disease in the cervix after irradiation was a factor in the lymphatic spread and the large number of patients with positive lymph nodes after radiation therapy.

The large number of associated pelvic abnormalities, particularly fibroids, endometriosis, and inflammatory conditions, encountered in this series contributed to the end results in no small part for both methods of treatment.

Some patients are technically inoperable, particularly the short, stocky, and frequently obese type. This body conformation makes operation difficult even in the most simple pelvic procedure and, when coupled with one or more of the above associated pelvic abnormalities, multiplies the hazard.

The large number of negro patients, 43 per cent, for the electively surgically treated group, and 55 per cent for the irradiated and surgically treated group contributed to this feature since the negro race is genetically prone to develop fibroids and sociologically disposed to pelvic inflammatory disease.

Summary

1. Eighty-six patients with carcinoma of the cervix were treated, 46 by elective surgery and 40 by radiation and surgery, and the results presented.

2. The over-all survival rate for the group treated by surgery was 59 per cent and for the group treated by radiation and surgery, 38 per cent.

3. Nine patients, or 20 per cent of those treated by elective surgery, revealed regional lymph node involvement by metastasis at the time of operation. One patient treated by radiation and surgery revealed positive lymph nodes.

4. Fifteen patients, or 38 per cent in the radiated and surgically treated group, showed residual cervical disease in the surgical specimen. Fourteen patients, or 35 per cent in the same group, had residual disease in the surgical specimen and metastasis in the lymph nodes.

5. Four patients, or 9 per cent in the surgically treated group, and 15, or 38 per cent in the radiated and surgically treated group, developed complications which were believed to be directly attributable to the surgical procedure.

6. Twenty-five patients, or 54 per cent of the surgically treated group, and 19 patients, or 48 per cent in the radiated and surgically treated group, had associated pelvic abnormalities.

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Discussion (Abstract)

Dr. J. O. Porter, Little Rock, Ark. My remarks will be brief, I assure you.

I want to compliment Dr. Cromer on his excellent paper and assure you that it has been a long, detailed, arduous task, preparing such a paper. Any of you who have done work like this know how time consuming it is.

I have no criticism to offer of the results, for they correspond very closely to the work done by other men.

I would like to show two slides reporting 108 cases from the University of Arkansas. We have arranged our material in a little different manner. You may

be interested in a comparative study. All of our cases, with the exception of 17, were post-radiation cases in contrast to Dr. Cromer's combined study.

In our review of 108 cases, were 17 patients who received no treatment. Twenty-one patients received palliative x-ray therapy, 22 patients had palliative surgical procedures. Some of these were operated upon with the intent of doing pelvic eviscerations, but nodes were found outside the pelvis and we stopped with palliative procedures, such as ureteral transplants and colostomy.

Twenty-two pelvic eviscerations were completed and in these 108 cases, 26 Wertheim procedures were done in post-irradiated patients.

In a series of 17 patients receiving no treatment the average survival was four months. Twelve per cent of these patients are still alive. With palliative x-ray therapy the average survival was six and a half months, a 10 per cent survival. In the palliative surgery group the average survival was seven and a half months,—16 per cent are still alive. In those having evisceration the average survival time increased to one year, 27 per cent are still alive, and of these, 5 are still alive for at least 5 years. In those having had Wertheim operations after irradiation, 69 per cent are still alive, the average survival being one and a half years.

Again I would like to compliment Dr. Cromer on his excellent paper.

Dr. J. Burch, Nashville, Tenn. I had not planned to discuss this paper, and feel a little embarrassed in discussing it because I am thoroughly confused. Perhaps I did not get the point in Dr. Cromer's paper about the compensation in the radiation and surgery group. I thought the surgical and radiation group was made up of patients some of whom had been irradiated as long as two or three years prior to the operation. Is that correct, Dr. Cromer? Was there any constant relationship between the time of irradiation and the surgery?

Dr. Cromer. There was no constant difference. They were irradiated and as soon as they got in the hospital, they were operated on.

Dr. Burch. What was the average interim?

Dr. Cromer. About six months.

Dr. Burch. Well, that clarifies one point in the thing for me. The second thing I would like to say is that it would be very unwise to draw any conclusions from a series as small as this one. Perhaps these results are correct. Certainly Dr. Mays thinks so, so does Dr. Farnswick. All I can say from my own experience is I do not believe they are correct.

Now, it has been my province to irradiate patients who have cancer of the cervix, giving them about 5,000 milligram hours of radium. The radium is distributed as 60 milligrams around the cervix, 60 milligrams in the fundus, and it is left in for not over 5,000 milligram hours. The filtration is about 1.5 mm. Now, with that irradiation and with that type of treatment, the cases are then operated upon at 6 to 8 weeks, never longer than 8 weeks after irradiation. I have not found the difficulties of surgery any greater in those than in nonirradiated cases, nor have I found that the fistulas are any greater, and the rectovaginal fistulas have been insignificant. In all of my work I have had one rectovaginal fistula. I have had urethral fistulas but I cannot see any difference here between irradiation and nonirradiation. The advantages of radiation in patients being prepared for surgery I think are pretty good.

One point that appeals to me about radiation is that it is a holding operation until you can get the patient in condition. Many of these women are short, stocky, and fat. You can give them a small dose of radium, 5,000 milligram hours, that is the dose McKelvie gave when he got his very good results. It is enough to kill an awful lot of these patients. During these 6 or 8 weeks, you can reduce them 15 or 20 pounds and bring them into the operable group, making the operation a lot easier. The other points, of course, are well known. Infection is controlled and the danger of transplants is lessened. Then there is always the fact that certain patients can be cured by irradiation, and certain ones can be cured by surgery. With our present media we cannot pick them out. Therefore, if we can devise a safe technic, and I believe the technic I have described is safe, it appears to me that the combined procedure has something to offer. I cannot give you the end results in statistics, but I can say they are a good deal better than those which have been presented today.

Dr. Bayard Carter, Durham, N. C. I am familiar with Dr. Cromer's work and have observed most of it. I think it is extremely interesting. I feel as he does, in contradistinction to Dr. Burch, that the Wertheim procedure is done much, much easier in the absence of previous irradiation. Perhaps I should modify that by saying that the Wertheim operations we have done following radiation therapy included deep x-ray treatment which I believe makes the procedure more difficult.

The only thing we should be concerned about as gynecologists is to get the cervix back into the realm of the gynecologist. I think it is a gynecologic condition and I think it belongs to this particular specialty. We should make efforts in that direction. I feel that the patients who do survive 5 years following surgery have been successfully operated on and many are living well beyond the 5 years. In the patients I have seen they are in much better condition, physically, and sometimes mentally, than the patients who have had extensive radiation therapy. Certainly long range complications have been much less in our hands.

Dr. Joseph W. Funnell, Oklahoma City, Okla. I wish to relate an incident that recently happened in Oklahoma City. We had a Society meeting to which we annually invite outstanding men in different fields to participate. A radiologist who is world-known was there. He stated in an open meeting that he would be glad to go anywhere in the United States at his own expense to testify against a man who would surgically treat carcinoma of the cervix.

To clarify my position allow me to state that, since I have become associated with Dr. Joseph W. Kelso and have had the opportunity to see personally the excellent results of a large number of cases of carcinoma of the cervix treated surgically, there is no doubt in my mind that this method is a valuable

addition to our armamentarium for the management of this lethal disease.

Dr. Cromer (Closing). This is a rather bad time to discuss cancer. It is the end of a busy day, and it has been a long session. It is too late for a lengthy debate on this subject, but I should like very briefly to rebut Dr. Burch's remarks.

The best that has been accomplished for cancer of the cervix by irradiation therapy is an over-all survival rate of about 40 per cent. Those patients are given a break.

Let us consider what happens to the remainder, the 60 per cent who do not get a "break." Those patients have Stage II, Stage III and Stage IV lesions; they are treated by irradiation, and in this series of cases they were treated consecutively, not selectively. There was a reason for the length of the interval between irradiation and operation. One can operate upon patients, it is true, who have had radium to the cervix 6 or 8 weeks earlier. When the patients have had external x-ray, transvaginal x-ray and radium therapy, however, surgery is sometimes very hazardous. It is my considered judgment, based on a large number of cases, that disastrous results can occur if one operates too early upon patients who have been heavily irradiated. (The patients in this series were all heavily irradiated.) There is quite a difference between just radium to the cervix on the one hand and external and transvaginal x-ray therapy and then radium on the other hand. These two types of treatment create entirely different surgical problems.

The 29 patients in our study with residual disease were in Stages II, III, and IV, and their diagnoses were all confirmed by microscopic examination. They represent residual disease in the cervix after irradiation. They were all irradiated accurately and adequately and then operated upon.

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An Evaluation of Histamine as a Therapeutic Agent in Some Allergic Disorders*

JOHNNY A. BLUE, M.D., *Oklahoma City, Okla.*

The use of histamine in the treatment of certain diseases of sensitization has fallen into disuse. A re-evaluation of its efficacy is offered by the author.

IN THIS ERA OF SCARCITY OF HOSPITAL BEDS and rapidly changing therapeutic measures, along with the introduction of more potent and, shall we say, dangerous drugs to our armamentarium, one naturally looks with favor and a sense of well being on a proven remedy that has less risk to the patient and doctor than some of the newer and more popular drugs, steroids and corticosteroids, in the management of some allergic conditions. Such a drug is histamine.

This paper will be devoted chiefly to the use of histamine as a therapeutic agent mainly in allergic conditions where the antigen antibody is not demonstrable. By this I wish to make it clear that, in my opinion and most of the leaders in the field of allergy, histamine is of no value in the treatment of hay fever, asthma, allergic rhinitis, allergic eczemas, and such conditions where antigens and antibodies *are* demonstrable.

Horton[1] has said that histamine will prove to be one of the most valuable drugs the allergist has at his command. This is not universally accepted. There is a feeling by some that histamine is a drug of considerable interest but of little therapeutic importance.

The steroids and corticosteroids have overshadowed many of the older therapeutic measures. While attending medical meetings and visiting with men in the field of allergy and reviewing the literature, one notes the paucity of histamine being used intravenously or by iontophoresis in allergic conditions where antigen-antibody reaction is not demonstrable, as in allergic migraine[2] headache, post-traumatic headache, Meneire's disease, urticaria, serum sickness, et cetera.

The literature[3] on histamine is voluminous. Most of it deals with arguments on its therapeutic value and its relation to allergy and anaphylaxis.[4] Much is said about subcutaneous injections for desensitization. There are a few reports on its intravenous[2] use and by iontophoresis.[5] However, these deal mostly with investigative and hospitalized patients.

Because of the inability to get beds in the hospital for patients having severe acute urticaria or serum sickness, and because of the expense and the lack of desire of some patients who were less ill, to be hospitalized; it was decided to give histamine to these ambulatory patients in the office.

Most of these patients were referred cases who had received the usual therapeutic measures, such as diet, calcium, sedatives, glucose, ephedrine, antihistamine,[3] ACTH, and cortisone.

Intravenous Administration

Two methods of administration were used in this series of cases, the intravenous, and iontophoretic. Because the procedure was for the ambulant patient it was decided to give one intravenous infusion daily of the 2.75 mg. histamine acid phosphate in 250 cc. of normal saline. No attempt was made to count the drops. The infusion was given rapidly enough to produce a lasting flush during the intravenous procedure. The time used averaged about one-half to one and one-half hours. Some could tolerate it rapidly and some had to receive it very slowly. As high as four ampules (2.75 mg. each) were added to one infusion in some patients to

*Read before the Section on Allergy, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

obtain the therapeutic results. No patient was found who could not tolerate 2.75 mg. if given slowly enough.

The patients in most instances sat in a chair and read while receiving the infusion. There were two or three who were permitted to hold the intravenous bottles and walk to the window and watch the traffic or a parade with the needle in the vein, on special occasions.

All were instructed to take some food just previous to the injection. If "heartburn" developed, an anti-acid was given during the infusion.

On the average, two daily infusions were advised. In the pencillin urticaria and severe serum sickness type of reactions, most patients were asymptomatic after four to six injections. Some received fifteen or more infusions.

The age ranged from 5 to 70 years. Children seem to tolerate the drug as well as adults.

After the patient was asymptomatic and the intravenous therapy was discontinued, bi- or triweekly subcutaneous injections of histamine 1:1000 solution in large enough dosages to produce a mild flush was advised as a maintenance dose for a week or so in some of the severe cases.

Histamine by Iontophoresis

A direct current apparatus was constructed using a Burger's radio dry cell 45 volt battery for current. A milliamperemeter, with a reading of 0 to 25 ma., and a rheostat to keep from giving a shock, were connected to the apparatus. An electrode was prepared by folding Reynold's aluminum Wrap 3 inches wide and 8 inches long. To this was attached the positive pole of the B-battery.

Three sheets of Kleenex are folded three times, and 3 to 5 cc. of a 1:100 aqueous solution of histamine dihydrochloride (Imido Powder)* is applied evenly to the Kleenex. This in turn is applied to the patient's forearm with the aluminum electrode held firmly over it by elastic bandage or gauze, being careful that the pressure is generalized and that no metal is touching the skin.

The negative pole was similarly constructed except that a thin rubber sponge is used under the electrode and is dampened with normal saline solution to permit the current good conduction. This is attached in a similar manner to the opposite arm. The current is then turned on and gradually increased to 8 to 25 ma. according to the patient's tolerance. In several minutes a generalized flush is produced. The current is left on 15 minutes. The flush remains several hours and has a tendency to recur several hours later. It may be assumed that by this method the patient receives approximately 0.065 mg. of histamine per milliampere per minute through the skin.

This is repeated twice daily for a period of 10 days on the average. If further treatment is necessary, the patient may be instructed to administer further treatment with the apparatus at home where he can continue the schedule at his convenience.

Discussion

Histamine rarely proves toxic in man. Excessive dosages will produce flushing followed by pallor, chilly sensation, metallic taste, pounding frontal headaches, rapid pulse and faintness, fall in blood pressure, visual disturbances, bronchial constriction, dyspnea, vomiting, coughing up of mucus, diarrhea, and in some cases, shock. Epinephrine will counteract these symptoms, however. In case of shock the normal blood volume should be restored.

There is increased flow of blood in the coronaries when histamine is administered, (we gave it to one patient who had had a coronary occlusion with no ill effect).

The site of action of histamine in the skin is the blood vessels where it causes dilatation and increased permeability.[6]

Histamine is potentially a strong activator of bronchiolar musculature. Its action is independent of and unaltered by atropine. It is believed to have little effect on the bronchi of normal persons, but is said to have very marked effect on persons with bronchitis, bronchial asthma, emphysema, and cardiac asthma. The violent dyspnea observed by some when histamine is administered intravenously is said to be due only partially to obstruction by muscle spasm of the bronchioles. Congestion and edema of the mucosa play a prominent part. (No such violent reactions were noted in patients in this series of cases studied.)

*Supplied by Hoffman LaRoche (Imido Powder).

It has been the consensus of investigators that histamine would precipitate attacks of asthma when administered to asthmatics. Prince and Etter[7] found that this did not hold true in their cases. In our series of patients with a past history of asthma, only two showed any increase in their asthma and this was only an aggravation.[8] In only one of the latter were the asthmatic symptoms of any consequence. This would seem to indicate that the administration of histamine injections is no determining factor in deciding if an individual has an allergic state.[8]

There are only one or two patients with a previous history of duodenal or peptic ulcer in this series; none had an immediate flare-up of the ulcer, one had a recurrence of the ulcer several weeks after the treatment was terminated. This latter phase of histamine therapy has been the cause of conflicting views.[2]

Horton[9] found that histamine desensitization for histamine cephalgia in patients with an ulcer produced an improvement. McHardy and Browne,[9] using this as a criterion, attempted to treat active ulcer cases with histamine desensitization, but found that it caused such marked aggravation of symptoms that the treatment was abandoned.

Horton[10] observed that many of the beneficial effects of ACTH and cortisone in clinical use have been paralled by histamine therapy. It is his belief that histamine therapy causes release of these hormonal agents. If this be the case, it would be logical to assume that histamine therapy would be the safer and more conservative drug of choice in the treatment of conditions where it has proven of value rather than resorting to the corticosteroids.

"Most workers, however, seem to agree that there are no major inconsistencies to the assumption that the fundamental allergic reaction is identical with that of the anaphylactic reaction, and that histamine,[4] as one of the by-products of this reaction, is casually related to most of the phenomena."[9]

"The majority of workers seem to agree now, that the source of the histamine is in the tissues of the sensitized animal and that it is released into the blood and lymph as a consequence of the antigen-antibody reaction initiated by the re-injected antigen."[9]

"Many of the factors and idiosyncracies of anaphylactic syndrome remain unexplained—it also appears clear that the cellular discharge of histamine does not account for all the phenomena of anaphylaxis. . . . Nevertheless the question of the involvement of the chemical is progressing from suspicion and circumstantial evidence to more direct and convincing proof that it plays the fundamental role in the anaphylactic reaction."[9]

Histamine itself is not antigenic and does not induce antibody formation and thus does not act as a means of specific desensitization. Most workers seem to agree that repeated exposures of animal and man to the amine diminishes the susceptibility of a tissue to this substance. Ramévez and St. George[11] in 1924 were the first to attempt desensitization to histamine by repeated, increased doses. Karady, Smith and Katzenstein also verified this. Horton[1] developed his method of treating histamine cephalgia cases. After repeated and increased doses of histamine, he found that on repeated attempts to induce this type of headache by the injection of histamine the patients had developed a tolerance, and each attempt

TABLE 1

AN EVALUATION OF HISTAMINE AS A THERAPEUTIC AGENT IN SOME ALLERGIC DISEASES (194 CASES)

Method of Administration	*Acute Urticaria Serum-Sickness*	*Chronic Urticaria*	*Migraine*	*Histamine Cephalgia*	*Vertigo*	*Traumatic Headache*	*Multiple Sclerosis*	*Psoriasis*
(INTRAVENOUS 165)								
Results:								
Cured	68	23		3	2	1	1	
Improved	18	20	17	3			1	
Poor								
Failure	2	4	2					
(IONTOPHORESIS 29)								
Results:								
Cured	7	5		1				
Improved	2	7		2		1		1
Poor	1							
Failure		1						

required larger doses to precipitate an attack.

"The mechanism by which the favorable effects of histamine therapy is produced is not well known,"[12] however, it is generally conceded that its action is that of increased tolerance of the tissue to the substance released during the allergic reaction.

Prince and Etter[7] are of the opinion that histamine by its dilating effect on all of the capillaries around a hive brings about an absorption of the edema fluid and facilitates ridding the body of it by diuresis.

Histamine increases the output of epinephrine from the adrenal medulla.[4]

The above information and data were the principal stimulating factors in the treatment and presentation of this series of cases (Table 1).

Summary and Conclusion

A series of 194 cases treated with histamine by the intravenous and iontophoretic methods is presented.

It is concluded that this type of histamine therapy is very beneficial in acute urticaria, acute serum sickness-like disease, chronic urticaria, allergic headaches, migraine, vertigo, traumatic headaches, multiple sclerosis and psoriasis diseases.

Iontophoresis seems to be the therapy of choice due to its simplicity of administration, the less time involved in the administration, and the more persistent flush following its use, because of the production of deposits of histamine in the pores of the skin by this electrical technic.[13]

Histamine is a safe, harmless, therapeutic agent and is practically a specific for the serum sickness type of allergic reactions.

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Discussion (Abstract)

Dr. Boen Swinney, San Antonio, Tex. Dr. Blue is to be congratulated for again bringing to our attention the proper use of histamine in the treatment of some of the allergic and related diseases. I have heard a number of physicians remark that they have discontinued the use of histamine because of its failure as a therapeutic agent. Likewise, I have seen many patients come through my office on whom histamine has been used without the proper indication, and in some who have had the proper indication the histamine has been improperly administered. If we would but review Horton's original and some of his subsequent reports on the indications and use of histamine and follow his line, I believe we would all become enthusiastic in its use.

I have not adopted iontophoresis, perhaps I should, the reason being that in the instances of serum sickness and chronic urticarias in which I have used histamine have usually responded to just a few doses of 1:100 histamine intradermally. Usually 0.03 cc. is adequate to produce a moderate flush reaction and most have cleared up with just a few flushes. In most patients who have histaminic cephalalgia and who require treatment over a period of weeks and months, I try to get away from office procedures. In these, I teach the intelligent patients how to follow out Horton's schedule of treatment subcutaneously.

One point I would make in the use of histamine is this: there are several different preparations and dilutions on the market prepared by various pharmaceutical houses. As I had considerable difficulty with patients who take home treatment in securing the preparation I desire, I make up the dilutions in my own laboratory and supply the histamine to them, thus I know they are getting the proper dilution and proper preparation.

Dr. Henry Ogden, New Orleans, La. We cannot state that all cases of headache which appear after the injection of histamine fall into the category of Horton's syndrome (histamine cephalalgia). We must remember histamine is a vasodilator, and vascular headache is associated with increased amplitude of pulsation in the vessels, and that vasodilation may be present. I think if we follow Horton's description we must be cautious about including many of these cases as being true histamine cephalalgia. In my paper I pointed out that the injection of histamine will produce different types of vascular headache. This includes not only headache of the intracranial type (due to dilation of the intracranial vessels), but migraine, frontal headache, etc.

The injection of histamine may produce a generalized type of headache very quickly. This headache may last for only a few minutes. In histaminic

cephalalgia, a typical attack may occur within an hour after the administration of the drug. Therefore, just because histamine can be shown to cause headache we cannot necessarily say that the patient has histamine cephalalgia.

Dr. Harris Hosen, Port Arthur, Tex. I used histamine routinely some years ago for migraine. In the first few cases, the results were wonderful, the next few gave fair results, the next few, no results. I stopped using it. Some years later, I started again on this basis by giving 0.035 cc. of 2.75 mg. histamine subcutaneously, and if I could produce a headache that was almost identical with the headache from which the patient suffered, I would use it intravenously and I think I am getting somewhere with it. In that way I differentiate those cases in which I should not get results.

As regards time, I find in migraine it takes, as a rule, four or five hours to get in 250 cc. of saline with 2.75 mg. of histamine in it. If I let it run as much as 30 drops a minute, intense headache often is produced. I give 2 cc. of adrenalin (1:1,000,000) intravenously and it stops the reaction. I am just wondering whether it is necessary to give the whole amount. If one stops in an hour or two, one gives one-third of the dose and may get the same results.

I would like to know if the speaker has had similar experiences in the long time necessary to give the histamine in the patients having headaches.

Dr. Blue (Closing). I mentioned that it does not make any difference about how long it takes to give it, what you want is the flush. I have had some patients in whom it took two to three hours to get it, and maybe longer than this sometimes. I think the longer one gives the histamine, the better results one is going to get, and the more constant the histamine effect will be. Of course, it is rather hard to keep a patient in the office and tie one room up for four or five hours every day, or twice a day, as I did. All these patients were given the treatment in the office. I have had some who have had headaches with treatment; one can give too strong a solution, and those are the patients with whom one has to be cautious. Someone must watch these all the time. In intravenous therapy the turning of the arm or something like that will increase the drops and I think a lot of times the reason one gets poor results is because one does not have constant watching of the patient. If the needle is against the wall of the vessel, not as much will be delivered as if it is turned up. I have had some patients do this themselves, and thus regulate the dosage. They get rather accustomed to those things. I think the constant getting of the histamine, whether by deposit or intravenously, is the thing.

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Allergic Problems in General Practice:

Question and Answer Period.*

MODERATOR: HOMER E. PRINCE, M.D., *Houston, Tex.*,
PANELISTS: MAURICE C. BARNES, M.D., *Waco, Tex.*, LAWRENCE J. HALPIN, M.D., *Cedar Rapids, Ia.*, SAM H. SANDERS, M.D., *Memphis, Tenn.*, and NORMAN W. CLEIN, M.D., *Seattle, Wash.*

Here is an opportunity for the general practitioner to get answers to some of his problems in the field of allergy.

MODERATOR PRINCE: We have a number of very good questions and a limited amount of time. I am going to proceed with the discussion without further introduction.

QUESTION: *What is the significance of high blood eosinophilia in the allergic child?*

DR. CLEIN: Blood eosinophilia is not constant in allergic conditions in children. About one-third of the allergic children with the major forms of allergy, such as asthma and hay fever, may show a transitory eosinophilia at one time or another. If it is there, it is of some diagnostic value; if it is not there, it does not change anything. Of course, the importance of it is that one must rule out worms and parasites of one kind or another, which are probably the chief cause of eosinophilia in children, as well as any other cause of eosinophilia.

QUESTION: *I have had one child give a local and generalized reaction to gamma globulin. I wonder how many others have noted this.*

DR. BARNES: I have not had any experience with reactions of that kind.

MODERATOR PRINCE: Has anybody had any experience of such reaction with gamma globulin? I will start out by saying some years ago we saw a typical case of foreign protein-type reaction from one injection of gamma globulin.

I was thinking of asking Dr. Blue. He is not on the Panel. Have you had any, doctor? I know you have done some work with foreign protein-type reactions.

DR. JOHNNY BLUE: *(Oklahoma City, Okla.).* No, I have not.

MODERATOR PRINCE: Has anyone had such experience? The person that asked this question, obviously, had one case. Has anyone else had any?

FROM AUDIENCE: I had one.

MODERATOR PRINCE: From human gamma globulin?

FROM AUDIENCE: Yes.

MODERATOR PRINCE: There is no reason why gamma globulin could not, with some chemical change, cause a reaction. Theoretically, it probably would not occur, since extraneous factors are supposed to be eliminated. Some ingested foreign protein in the way of food could enter into the patient, I should think. I believe we will accept the fact that it has occurred. There is nothing one can do for it other than routine treatment of the type mentioned by Dr. Blue in his paper, "An Evaluation of Histamine as a Therapeutic Agent in Some Allergic Disorders," (pp. 636-640) if it is serious enough to be required.

QUESTION: *Is Thorazine a sensitizer by contact?*

DR. BARNES: Yes, I think it is. I, personally, have not seen one. I have talked to men who have. I have seen a number of allergic reactions from the internal use of Thorazine. The men at the Veterans Hospital in my city are using quite a bit of it now and I have had occasion in my clinic out there to see a number of patients who got a generalized skin eruption from it. I think it is a fairly common sensitizer, both as a contact agent and internally.

*Held before the Section on Allergy, Southern Medical Association, Forty-Ninth Annual Meeting, Houston, Tex., November 14-17, 1955.

MODERATOR PRINCE: Does any other member of the Panel want to add anything to Dr. Barnes' remarks?

We had two nurses from the same nursing station at a hospital in Houston who had a contact dermatitis from Thorazine. Even after they were instructed to wear rubber gloves when they handled it, they continued to have trouble. We finally found out that some other nurse would handle the Thorazine and then the charts at the chart desk, and the nurses were getting the contact there. It required about thirty days for both of these people to clear up after absolute removal of the Thorazine.

QUESTION: *Are nasal polypi on an infectious or an allergic basis?*

DR. SANDERS: Both. I think we definitely have polypi due to infection and allergy. There are a lot of ways in which one can decide whether the polyp is due to infection or allergy. The first and most important is the history, because if you have a history of allergy, naturally you are suspicious of the polyp being due to the allergy. The second is the location. Most polyps due to allergy will occur between the septum and the lateral wall of the nose, while the polyp caused by infection is in the middle meatus or originates from one of the sinuses. In other words, where we have a polyp in the middle meatus, it might be due to the ethmoid. If we have a polyp coming from the antrum, it will be hanging out of the middle meatus or in the nasopharynx.

A very definite aid in making a differential diagnosis is the use of x-ray, nasal smears and nasal findings. If we have a patient with a history of an obstructed nose, we see the polyps in the nose and there are so many of them we cannot tell where they are coming from. When you x-ray that person, if it is allergy you will have a generalized density in all of the sinuses, not necessarily a marked density, but there will be evidence of uniform changes in the lining mucosa. If he has an infection, there will be a thickening of the mucosa of the sinus, heavier near the bone and gradually shading out until we see the edematous surface mucosa. If it is an infectious process, it is not likely to be uniform. There will be more density in the one maxillary sinus, more in the ethmoid, or maybe more on one side. In hypertrophic sinusitis where we do not have any pus yet due to an infection, we will see a uniform thickening but there will be more density than occurs in allergy, and that density may be limited to one sinus or more than one sinus.

There is no doubt that all polyps in the nose are due to either infection or allergy, and we must differentiate between them before we know where to begin treatment.

MODERATOR PRINCE: I think your first statement that polyps are often due to both is quite appropriate. Do not overlook the fact that bacterial infection is antigenic quite frequently and of course in this instance, as Dr. Sanders has pointed out, the infection is active locally.

QUESTION: *What do you use as a substitute for ephedrine in asthmatic men who have prostatic constriction and urinary retention from taking ephedrine?*

Dr. Halpin, would you care to comment on that?

DR. HALPIN: Usually I would substitute aminophyllin or other xanthine derivatives for the ephedrine. Personally, I do not use much ephedrine in elderly asthmatic men so I think that I would use a xanthine derivative in place of it.

MODERATOR PRINCE: Have you seen any of the synthetic ephedrine-like drugs, such as Propadrine, cause this condition, Dr. Halpin?

DR. HALPIN: Not in my experience.

MODERATOR PRINCE: I do not believe Propadrine causes it frequently, if at all. In other words, substitute another drug if you can.

QUESTION: *What are some good tar substitutes to use in chronic eczemas with lichenification in patients who are sensitive to tar?*

Dr. Barnes, do you see that as a problem? I am sure you do.

DR. BARNES: Yes, I think we do. I do not think tar is a particularly frequent sensitizer. Most patients will tolerate it reasonably well. In fact, if I had to place it on a list of sensitizers, it would be low on the list. Occasionally, of course, you will run into that problem. When you do, you may substitute salicylic acid in various strengths, about 2 to 6 per cent, depending on the thickness and lichenification in the skin and your estimate

of the patient's tolerance for it. That would be one of the best choices of substitutes,—salicylic acid ointment instead of tar.

QUESTION: *Should antihistamines be routinely used in allergic rhinitis?*

DR. CLEIN: They should be given a trial in all cases, not only in allergic rhinitis but in other types of allergy in children. I wish I could say they are as effective as the advertisements state. Sometimes they do help and they are an aid along with the rest of the treatment. Even if the child is relieved of his symptoms by the use of an antihistamine, the allergic study should be continued. We found in many small children whose hay fever was relieved during the pollen season, that these children later developed asthma. The antihistamines will sometimes make them look fine on the surface but their allergy is piling up inside of them. So even if they are relieved, it should not preclude further treatment.

MODERATOR PRINCE: I thoroughly agree with your remark. We think we are seeing more pollen asthmas since the patients mask their hay fever symptoms by the use of antihistamine preparations. All of a sudden they break down in asthma.

Dr. Sanders, perhaps since you have been talking about infectious problems in the nasal area, you might answer this one.

QUESTION: *Which of the antibiotics or chemotherapeutic agents do you find best for continuous antimicrobial therapy when you decide to treat a patient with such a drug?*

DR. SANDERS: I think that all, or practically all of them are about the same. One will get less side effects by using a large amount of B-complex or the stress formula with the various mycins. I hate to use a trade name but Mysteclin in my experience has been very satisfactory when a mycin is given over a long period of time. If the mycins are used over a period of five days, we add the B-complex factor and if the patient complains of fatigue after taking an antibiotic for a good while, we use B-complex intravenously. For some reason, the patients do much better.

MODERATOR PRINCE: Dr. Clein, do you put any of your infected children on continuous use of any antimicrobial preparations?

DR. CLEIN: No, I do not keep any of them under constant treatments, because I firmly believe that once children have their allergic problem corrected, then if they do catch a cold they get over it just as any non-allergic child. I do not use any type of antibiotic or antimicrobial preparations routinely because once the allergy is corrected, infection is not a factor. They get over their colds just like any other child. I do not believe that bacterial allergy is much of a factor in children.

DR. SANDERS: May I add something just to clarify that? We have used the various antimicrobial preparations for experimental purposes in atrophic rhinitis and in certain diseases we have not been able to do anything with.

I agree with Dr. Clein, when we are dealing with allergy and some superimposed infection, that we should cut off the medication as soon as possible. However, in middle ear infections and sinus infections, mycins should be given over a longer period of time than in ordinary acute infections if we expect to get results. However, one finds a lot of instances of middle ear disease with involvement of hearing, in which antibiotics were given (mycin drugs) for three or four days, then discontinued with a recurrence. We feel that all antibiotics should be given in adequate doses to entirely eradicate the infection. The hearing should be checked to determine if there has been any damage to the hearing.

MODERATOR PRINCE: Your Moderator belongs to the school that feels that infecting agents, bacteria, frequently constitute the allergens, particularly in children. Under certain circumstances, after we have exhausted other allergy approaches and have assumed the existence of, let me say, bacterial allergy, we have employed some of the antimicrobial agents. We prefer not to skip around, first with one and then the other, for the fear of building up too many resistant bacterial strains. We have used the sulfonamides, in low dosage, over quite a long time, with the usual precautions and watching the patient.

There is another part to this question: *What are your feelings regarding penicillin sensitization?*

Dr. Blue has covered that in his paper (pp. 636-640). I presume the questioner wanted to know whether you would repeat the drug in the face of a previous reaction. I would

say in the case of a critical condition in which penicillin would be the only choice, I might repeat it provided the previous reaction had been not too alarming, or I might repeat it under the protection of antihistamine preparations or even of corticosteroids.

DR. HALPIN: When there are other antibiotics capable of doing the job, it is wiser to substitute that antibiotic than it is to use one to which the patient has shown a reaction. I know of no instance where penicillin is the only antibiotic that would be effective.

MODERATOR PRINCE: I kept from getting on a limb there by saying if penicillin were the only drug we think would be effective in a critical condition. I feel the same as you do otherwise.

DR. CLEIN: Dr. Prince mentioned something that I think is very good. He mentioned the sulfonamides. I think they are still the safest, best and cheapest drugs for acute or chronic infections in children, better than any of the others.

MODERATOR PRINCE: Dr. Clein, do you think that the detail men are pressuring us into such high-geared medicine that we forget some of those that we know are good, potassium iodide, for example?

DR. BARNES: Mr. Moderator, may I make a comment here? I think many times our opinion of a treatment procedure or medication is determined largely by the type of practice we are doing. As a dermatologist I have a wholehearted fear of sulfonamides just as I have of penicillin. In fact, I never prescribe either penicillin or sulfonamides externally. I see as many reactions from the sulfonamides as I do from penicillin. Dr. Clein, I put the sulfonamides in the same boat with penicillin.

MODERATOR PRINCE: Dr. Halpin, discuss the prophylactic use of antihistamines in prevention of allergic reactions with emphasis on drug and transfusion reactions.

Now, this might require all day, but can you make a thumbnail comment on it?

DR. HALPIN: In a patient who has had a history of transfusion reactions it may be advantageous to use one of the injectible antihistamines in association with the transfusion. However, I would not give a drug to a patient who has a known sensitivity to that drug. I do not depend upon injectible and oral antihistamines to control any possible reaction. I would substitute another drug than the one that originally caused the reaction.

MODERATOR PRINCE: Dr. Clein, what is the best means in your experience of handling the problem of vomiting in a child with acute bronchial asthma, especially where it is aggravated by epinephrine and aminophyllin? What is the effect of Thorazine?

DR. CLEIN: We have used quite a bit of Thorazine in these children. If they cannot keep down fluids and are vomiting their medicines, they will also vomit Thorazine. The simplest and best treatment is to hydrate them, either by giving them retention enemas, which work very well in small children, or intravenous therapy and plenty of warm moist air. Steam in the air, plus hydration, will usually stop vomiting faster than any other medication.

MODERATOR PRINCE: Have you ever practiced medicine in the country and told the patients over the telephone at night, talking yourself out of a call, to use a little white Karo syrup with water by rectum? It works fairly well sometimes.

DR. CLEIN: We always have them put a teaspoonful of sugar in the 4 ounces of water, say, every three or four hours. I do not know whether it does any good but they retain it and they seem to improve.

DR. HALPIN: Dr. Prince, I think one thing ought to be mentioned here about vomiting in childhood asthma, although not to the degree inferred by the question. Some vomiting in severe childhood asthma is quite an advantage. The patient usually gets better, anyway.

MODERATOR PRINCE: Let him vomit, and then later control the vomiting.

QUESTION: *Has a high protein diet been found to be of value in combating recurrent respiratory infections?*

DR. HALPIN: I think my answer to that would be a simple no.

MODERATOR PRINCE: What do you think about it, Dr. Sanders?

DR. SANDERS: I cannot say.

MODERATOR PRINCE: How about you, Dr. Clein?

DR. CLEIN: We advise all of these mothers

to give the high protein diets. We stress that for all of the time, whether they are sick or not, I do not think it makes much difference since they never follow it anyhow.

MODERATOR PRINCE: I often wonder if we sometimes do not remove first one food and then another from a child's diet, particularly a little fellow who is growing and needs protein, and get him on almost a starvation program, interfering with his nutrition and his replacement of blood protein to form his own antibodies. I believe that a person should take as high a protein diet as his allergic capabilities will permit and of a varied nature. That is just a generality.

QUESTION: *Will Alternaria therapy alone serve in hyposensitizing against Aspergillus, Spondyllocladium, Hormodendron or Helminthosporium?*

MODERATOR PRINCE: The answer is no against Aspergillus. Since the other molds the questioner mentioned, as well as Alternaria, are in the same botanical group, Alternaria usually protects against sensitizations to them. Occasionally, an individual will have a specific sensitization to Spondyllocladium or to Helminthosporium, but I have never seen one to Hormodendron which Alternaria would not control. In other words, you are dealing here with family sensitization.

QUESTION: *What about the child whose allergic symptoms always follow upper respiratory infection? Is there anything you could add to the remarks that have already been made here?*

DR. CLEIN: This is the old discussion as to whether there is such a thing as bacterial allergy,—that is, similar to the allergy caused by eating egg and producing asthma. In my experience with these children, whose mothers say, "He never gets asthma until he gets a cold," once their allergic problem is under control they get colds but without asthma. In those children who do have frequent colds and bacterial infection influenza vaccine is very satisfactory. Two shots, given a week apart, seem to be more effective than the autogenous and stock vaccines that we have used, and it is quick and simple.

MODERATOR PRINCE: *What is the best permanent treatment of chronic eczema in infants and children?* I will clarify that question. I assume the questioner by the use of the word "permanent" means, what is the best approach to get to the underlying background.

DR. BARNES: I assume, as Dr. Prince does, the questioner is concerned with what diagnostic approach is best and what we should do with these children having eczema.

Of course, as you well know, we cannot outline any stereotyped rules for permanent topical treatment or internal treatment. The type of treatment will depend upon the stage at which we see the eruption.

If it means permanent management, there again we must go back to our allergic management. I think every child with eczema existing any length of time, certainly is entitled to, and must have a complete allergic survey and workup. If we can control his allergy, certainly his eczema is going to get better.

I am not at all impressed with topical treatment alone in these youngsters; at least it is usually disappointing in my hands. I do not think we get good results with just topical treatment alone. I belong to the school which believe it is on the allergic basis and I can show you cases in my office that will clear up dramatically with the removal of some offending substance like milk, egg, or probably some other allergen. I think the most important thing is a complete allergic survey. Try to get the child into proper allergic balance and the eczema is going to improve. It will not become so important then whether we are going to use a 2 per cent tar ointment or a 5 per cent tar ointment. Does that answer your question?

MODERATOR PRINCE: I think you have covered it, Dr. Barnes.

QUESTION: *How do you feel about the use of x-ray treatment in asthma not responding to dietary elimination, inhalant desentization, and injection therapy?*

Dr. Halpin, would you want to make a comment on that?

DR. HALPIN: I have had no experience with it because I do not use it.

MODERATOR PRINCE: Have you used it on any children, Dr. Clein? It has been recommended, you know.

DR. CLEIN: We used x-ray therapy about 15 or 20 years ago but we have not used it

since because our allergic treatment is better and more permanent.

DR. BARNES: I have had some experience with it, Dr. Prince. I do not think x-ray is an agent that should replace other methods of treatment by any means. The use of x-ray treatment in bronchial asthma is not new. Certainly as far back as fifteen or twenty years ago there were some men using it, and there is still an occasional doctor who will give x-ray therapy.

If it is given wisely, and in selected cases, I can see no harm in it, and at times, there is no question about it, it is quite effective.

I can recall several patients, perhaps ten or twelve years ago, of rather severe status asthmaticus, who had failed to respond to the usual measures. Their doctor sent them to my clinic for x-ray therapy and that is all. He wanted them to have x-ray therapy. As you probably know, those of you who are familiar with the dosage and technic of giving it, such patients get very, very small doses of x-ray. These particular patients were completely free of asthma for about six months, on about three x-ray treatments given through the mediastinal area. They were given about 100 roentgens at each treatment.

MODERATOR PRINCE: You were treating enlarged hilar nodes, and that sort of thing then, is that right?

DR. BARNES: I do not think that is a criterion for treatment. So far as I know, nobody has scientifically explained exactly what x-ray does in these cases, but at times it certainly may be very effective. I think the one thing to be emphasized is the question of safety and be sure the man who is giving the x-ray therapy is a good radiologist.

MODERATOR PRINCE: We have been under the impression that enlarged hilar nodes mechanically aggravate asthma in chronic respiratory infections. We have been able to help an occasional case of this type with x-ray therapy as an adjunct to other therapy. I agree with what Dr. Barnes has said. From my limited experience with x-ray, I cannot see any justification for giving x-ray treatment in heroic doses in other areas of the body rather than over the chest. On the other hand, I have seen pulmonary fibrosis follow too much x-ray over the chest. We would get into an awkward situation here, too. The x-ray is potent therapy and one that must be used with care and I would say extremely rarely. Dr. Sanders, did you want to say something about x-ray?

DR. SANDERS: I just wanted to call your attention to the work that is being done in Chicago now. Recently, they have picked up a number of cases of primary carcinoma of the thyroid in children, very young children, and of the twelve cases that were picked up, every one of them has had x-ray therapy of the upper respiratory lymphatics, tonsils and adenoids. I think this observation is very important and we should consider it before we give too much x-ray.

MODERATOR PRINCE: We must regard x-ray therapy with the greatest respect.

DR. BARNES: I would like to make one more observation about that. I have heard that for many years and I do not believe a word of it. I do not believe that x-ray therapy given with the proper technic and in the proper way produces pulmonary fibrosis. It is the inflammatory reaction in the tissues that produces the fibrosis. I have had considerable experience with both superficial and deep x-ray therapy. I have heard at different medical meetings, from time to time, "Oh, look at what he has done with x-ray, produced a fibrosis, this sequela or that complication." Most of the time that is voiced by a man who has had very little experience with x-ray therapy. I maintain and insist, if it is given properly, there is no element of danger in it, and is perfectly safe therapy.

MODERATOR PRINCE: Do you think the danger comes from these patients drifting from one man to another.

DR. BARNES: There again it is the responsibility of the attending physician to determine whether or not the patient has had previous x-ray therapy; and if so, how much he has had before he is given any treatment at all.

But, remember, if you know anything about x-ray therapy, you give these patients about 75 to 100 roentgens of filtered radiation. That is an extremely small dose. You do not get into the dosage used for malignancies or carcinoma. Yes, with carcinoma of the lung and deep x-ray therapy, you might get fibrosis, but not in the therapeutic doses that we use for bronchial asthma.

MODERATOR PRINCE: Dr. Barnes, I think we have seen some individuals who, we would have to assume, did not get the x-ray treatment properly. That is the type of thing I think demands the caution.

DR. BARNES: That situation, in both superficial and deep x-ray therapy, is what we have to fear. Dr. Prince recently told me of a traveling salesman, with a chronic, recurrent dermatitis of the hands. This patient got temporary relief of the dermatitis by x-ray therapy. Consequently, he would see a new doctor in each town and possibly get more x-ray therapy. In situations of this type, one may get too much x-ray. A doctor who would dare give an x-ray treatment, unless he has predetermined whether the patient has previously had x-ray therapy and if so how much, is treading on extremely thin ice.

DR. HALPIN: In that regard, Dr. Barnes, is the dosage of x-ray for any skin lesion an individual thing? I mean you have ten patients, let us say, with so-called eczema of the hands, or hand dermatitis. If it is your intent to use x-ray therapy, you cannot take all ten patients and give them the same dosage of x-ray even though none of them has been previously treated.

DR. BARNES: That is quite true, depending on the inflammatory reaction present, the texture and type of skin, the dosage will vary somewhat.

DR. CLEIN: The University of Chicago group also reported five cases of carcinoma of the thyroid in children who had had previous x-ray treatment for thymic disease. I have seen studies in other parts of the country of a large number of cases treated by x-ray over the thymus and in which no later sequelae appeared.

MODERATOR PRINCE: On two occasions I have had anaphylactic reactions to Adrenalin in minimal doses in children of 4 years and 11 years. The product was made by Winthrop Stearns. How often does this occur and how would immediate treatment be carried out?

DR. CLEIN: I have not seen any trouble with Adrenalin given by hypo. I have had trouble giving it intravenously in too concentrated amounts.

MODERATOR PRINCE: Has anybody else had any experience with this type of reaction? I think it occurs extremely rarely. I can recall two instances in each of whom I had obtained a history that previous injections of Adrenalin were not tolerated. I suspected that these two patients were morphine addicts and wanted morphine; instead I gave them Adrenalin in a dosage of 0.25 cc. In each instance there resulted a peculiar violent more or less collapse type of reaction,—that is the best way I can describe it. I do think such reactions occur rarely.

FROM THE AUDIENCE: Might that not be a vasomotor reaction?

MODERATOR PRINCE: I did not do anything but let them lie down and they got all right, fortunately. The next time I did not give them Adrenalin.

FROM THE AUDIENCE: I think that is a vasomotor reaction, as if you gave them Novocaine, don't you think so, Dr. Prince?

MODERATOR PRINCE: It might be.

DR. HENRY OGDEN *(New Orleans, La.)*: I had a girl of seventeen who was given an ordinary dose of epinephrine and died within two or three minutes, whatever the cause was. I remember an article in the *New York State Journal of Medicine* about seven or eight years ago pointing out that such reaction to epinephrine was a cardiac reaction. We did not have a "post" on this girl; we do not know the cause of these deaths from epinephrine.

MODERATOR PRINCE: I think it occurs, and there are people who cannot tolerate epinephrine. I do not understand the mechanism.

QUESTION: *What is the Panel's experience with Histopon?*

MODERATOR PRINCE: Histopon is a long-acting histamine, I believe. This question is addressed to the entire Panel; has any member of the Panel had any experience with the preparation?

DR. HALPIN: I have had none.

MODERATOR PRINCE: The Panel has no comments on the use of Histopon and I have not used it either. Has anybody in the audience used Histopon? Dr. Blue, have you used it in your histamine work?

DR. BLUE: No.

MODERATOR PRINCE: Would the questioner like to make any comments about that?

DR. GEORGE OWEN *(Jackson, Miss.)*: The

reason I asked the question was because of Dr. Blue's remarks in his paper (pp. 636-640), wherein, I think, the question was asked whether histamine ever produced asthma. In my first experience with Histopon I gave one dose; on the second day I gave another, and before I could turn around and lay my syringe down on the table the patient was in violent asthma. I just wanted to know if anyone had had any similar experience with it.

MODERATOR PRINCE: I assume from the reaction of the audience and the Panel that no one has had any experience with it.

QUESTION: *Please discuss the relative toxicity of cortisone and ACTH given to severe asthmatic infants. Does the growth phenomenon increase or decrease the dangers of such untoward effects as osteoporosis?*

DR. CLEIN: I never use ACTH or cortisone more than a week at a time in any of these children. I feel if one has to use it longer, or if it is used longer, one should resurvey, or reappraise the allergic management of the child. This needs improvement. We find it may be necessary to use it for a week or two to help the patient over a severe period. I have heard reports that some patients have died from large doses of these hormones over a long period of time. I find if I use them for a week or two, I do not encounter any of these troubles. I do not know much about osteoporosis or the other problems that were mentioned.

MODERATOR PRINCE: We have seen one instance, not in an infant, but in an adult, a negro nurse, with severe asthma. We had exhausted our usual procedures for relief and were getting ready to give her ACTH when she asked if the drug was ACTH. When answered, yes, she told us that in Detroit someone had given it to her by hypodermic injection and she had suffered a severe anaphylactic reaction. We then tested her with a very high dilution and obtained a large wheal with pseudopods. We did not give her ACTH therapeutically, of course; I think had we done so we would have had a dead nurse on our hands.

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EDITORIALS

CONSTRUCTIVE MEDICINE

Medicine, since the beginning of history, has emphasized two broad areas in medical care,—preventive and curative. Greater emphasis has been placed on the curative or therapeutic since it represented a struggle between death and survival. Curative therapy is spectacular: arsenic for syphilis, quinine for malaria, antibiotics and chemicals in the treatment of bacterial infections, and cardiac surgery, to name only a few. These are magnificent accomplishments, saving lives and lengthening the useful life span of millions of people. These "accidents" to the human body in terms of disease appear to be inevitable. Once recognized their correction becomes a matter of immediate concern.

The above approach is not so direct in the preventive field. First there had to be found the cause of illness, as in smallpox, dysentery, typhoid fever, diphtheria, rickets, pellagra and many other scourges of the past. Their elimination was effected by applying sanitation, active and passive procedures in immunization, and addition of vitamins in the respective diseases. There remain diseases to which these principles may well apply,—congenital anomalies, prematurity, cancer, rheumatic fever, and mental illnesses including criminal behavior.

As the physical illnesses appear to diminish in numbers, mental and abnormal behavior appear to be increasing. And just as the insidious symptoms of tuberculosis, cancer, and malnutrition are recognized, so should the attitudes of maladjustment become obvious to the physician. This is particularly true in the younger age group. It is recognized more and more that the pattern for delinquent behavior is laid down in the preschool and early school years. This is also the age in which the child is most frequently under the eye of the family physician and pediatrician, though no physician is immune to this exposure.

Since we assert our right and privilege to "treat" psychologic deviations, it is our responsibility to use measures just as strong to prevent them as we do in prescribing D.P.T. or vitamins. In the development of this "sickness" of the mind and soul, many environmental factors play a major role,—economics, schools, parental neglect of recreational facilities, disrespect of adults for legal prohibitions, and the like. Abnormalities in behavior do not at first glance spell medical interest, but they do spell future inmates of psychiatric and penal institutions. They challenge our interest and active participation in individual discussions with parents and in community planning for the *constructive* upbringing of children.

P. A. McLendon, M.D.

EFFECT OF SODIUM LACTATE ON CARDIAC ARRHYTHMIAS

Increasing cardiac rhythmicity through the use of molar sodium lactate has been a problem under investigation by Bellet and his associates[1-3] at the Foundation for Cardiovascular Research in Philadelphia.

Previously the drugs effective in increasing the ventricular rate in certain arrhythmias have been in the main of the sympathomimetic and vagolytic variety. Such drugs carry the danger of inducing serious ectopic rhythms. The effect of molar sodium lactate is probably on a basis of an entirely different character than these other agents. In addition to its experimental trial in a few human volunteers, the drug has been used in 46 patients presenting sinus bradycardia, partial and complete auriculoventricular heart block, Stokes-Adams seizures and in terminal cardiac arrest.

For years one-sixth molar sodium lactate has been used in the management of acidosis of various causes. More recently the molar solution has been used. The lactate is oxidized or is converted to glycogen. The sodium freed thereby is excreted in the urine as a bicarbonate, leaving an alkalosis of the base bicarbonate and raising the blood pH. Though the authors are not satisfied with any explanation of the effect of the drug on the heart muscle, they do not believe that the small amount of liberated sodium is sufficient by its excitatory effect on the myocardial cells to account for the accelerated heart rate. Rather

they are inclined to accept evidence in the past for acceleration of conduction and increased irritability of heart muscle as the result of the alkalotic state. There is the added fact that lactate is a readily utilized fuel for the cardiac muscle.

In young normal volunteers 100 to 200 cc. of the solution given in 10 to 15 minutes produced no untoward reactions; there was no change in pulse rate, blood pressure nor in the electrocardiogram though there were changes in sodium, potassium, chlorides, lactic acid, carbon dioxide and pH. Using molar sodium lactate in the treatment of conduction disturbances or arrhythmias, the authors used doses of 100 to 160 cc. in 10 to 15 minutes. In the treatment of cardiac arrest 17 cc. were given in 30 seconds and up to 500 cc. over a period of four to five hours.

The drug has been used in three instances of sinus bradycardia with rates of 30 to 40 per minute. These rates were raised by 50 to 75 per cent following the injection of the solution. In six instances of partial auriculoventricular block, five having sinus rhythm and one auricular fibrillation, with rates of from 32 to 50 per minute the rates were increased by 50 to 100 per cent.

Twelve patients having complete auriculoventricular block were treated with molar sodium lactate. In four the ventricular rates were increased accompanied by a comparable increase in the auricular rate. In three having auricular fibrillation the rates increased in the order of 25 per cent. Three patients having complete block and hyperpotassemia showed dramatic increases in rate under treatment,—15 to 100, 28 to 71 and 30 to 52 per minute respectively.

In instances of cardiac arrest molar sodium lactate has at times been dramatic in its results. The authors have had the opportunity to use it in four patients with standstill in Stokes-Adams attacks. In one patient it was effective in 10 episodes restoring the beat each time, though the patient eventually died in an attack when there was delay in treatment. In two it was successful in repeatedly controlling attacks of standstill; these patients were still alive six weeks after treatment. In the fourth patient asystole had been present six minutes before the injection; ventricular contractions were restored but the patient died. In the patients treated repeatedly, it was learned that no Stokes-Adams attacks might recur for about two hours. From their limited experience the authors advise for these attacks the injection of 20 to 80 cc. within a half to two minutes. Treatment should be given within the first two minutes of the asystole to make recovery more likely. Then to prevent further episodes the solution should be given by intravenous drip for some 6 to 12 hours at a rate of 15 to 20 drops per minute, the rate being increased if there is a tendency to recurrence of attacks. Electrocardiographic control is essential.

For study purposes 12 patients with terminal cardiac arrest were treated and electrocardiographic observations were made. These were in patients dying of uremia, carcinoma or acute myocardial infarction. It was learned that if the injection was given within one to two minutes of standstill the ventricular rate was again re-established. (In one it continued for nine hours before death; in another it continued as long as artificial respiration was maintained.)

These studies with molar sodium lactate are of interest and have a practical application. Though the effect of a single injection lasts only several hours, it appears that this drug has a definite place in the control of cardiac arrest of the Stokes-Adams type, tiding the patient over a period of such attacks. It seems particularly efficacious in controlling the bradycardia of hyperpotassemia. In an addendum to their last paper the authors note that molar sodium lactate has been successful in the resuscitation of three patients who developed cardiac standstill in the operating room during some types of operation. Thus, this drug which is without any side-effects, except for some premature contractions, may find a place on the anesthetist's table. We shall also await with interest the results of studies being made by the authors of the oral use of the substance in the control of Stokes-Adams attacks.

EDITOR.

References

1. Bellet, Samuel, Wassermann, Fred, and Brody, Jerome I: Effect of Molar Sodium Lactate in Increasing Cardiac Rhythmicity, Tr. A. Am. Phys. 68:161, 1955.
2. Bellet, Samuel, Wassermann, Fred, and Brody, Jerome I: Further Observations on the Cardiovascular Effects of Sodium Lactate: Effect in Normal Subjects and in Various Arrhythmias, Am. J. M.Sc. 231:274, 1956.
3. Bellet, Samuel, Wassermann, Fred, and Brody, Jerome I: Effect of Molar Sodium Lactate in Increasing Cardiac Rhythmicity: Clinical and Experimental Study of Its Use in The Treatment of Patients with Slow Heart Rates, Stokes-Adams Syndrome and Episodes of Cardiac Arrest, J.A.M.A. 160:1293, 1956.

CANCER QUACKERY

The Editor is duty bound to refer to a paper[1] which appears in this issue. It points up the collective responsibility of the medical profession in attacking a disgraceful situation.

Though most of the readers of this *Journal* unquestionably know that cancer quacks are in business in this day, it is doubtful that they know how extensive the business is. A dramatization of this charlatanism as done by Horton and his associates serves an important purpose in awakening an awareness of the damage done and pricking our conscience as to our duty.

If, in one institution and over a relatively short time, a series of cases such as is described here comes to the attention of the staff, one can only wonder how many times this group of cases can be multiplied in the southern states.

The authors have located the cancer quacks of their area and have had the interest to delve into the nostrums used by them in the treatment of new growths. They have learned that all those practicing cancer quackery are not necessarily dishonest. Some of the backwoods practitioners have firm faith in their remedy and treat without monetary return. Though this is true of a few, it is most probable that the majority of cancer quacks are basically dishonest and aware of the shortcomings of their treatment. In addition there are such notorious quacks as Hoxsey who has made the headlines time and again, Lincoln also widely known, and in the past the ill-famed Koch, now an expatriate to enjoy his ill-gotten gains. Koch's cancer cure, a "cure" also for many noncancerous diseases, continues to be distributed widely, and even occasionally to members of our profession. The paper by Horton and his collaborators is further enlightening in calling attention to a monthly magazine "The Defender" which seems to have as one of its purposes the advertising of these quacks and, as another purpose, attacking the medical profession for its opposition to charlatanism on the alleged basis of selfishness for pecuniary reasons.

We are glad to read that for the first time in recent years a "public warning" has been issued by the Food and Drug Administration, on April 4.[2]

> This public warning says in part: "The Hoxsey treatment costs the patient $400 plus $60 in additional fees; expenditures which will yield nothing of any value in the care of cancer. It begins with a superficial and inadequate examination of the patient at the Hoxsey Cancer Clinic, Dallas, or Portage, Pennsylvania. . . .
>
> "The Food and Drug Administration has conducted a thorough and long-continuing investigation of Hoxsey's treatment. His claimed cures have been extensively studied and the Food and Drug Administration has not found a single verified cure of internal cancer effected by the Hoxsey treatment. In addition, the National Cancer Institute of the United States Public Health Service has reviewed case histories submitted by Hoxsey and advised him that the cases provided no scientific evidence that the Hoxsey treatment has any value in the treatment of internal cancer."

At times we of the profession become a bit impatient with laymen when in their ignorance they give in to the "fast-talking" quack. However, with years in the practice of medicine one finally ceases to be surprised by the apparent irrational behavior of our patients. What is surprising though is the attitude of an occasional, presumed astute law-maker who in the Congress or in state legislatures arises to extol a cancer quack, or to attack the medical profession for its opposition to quackery with the ever-ready criticism of monetary loss as the basis for its attack on charlatanism. The ignorant patient who grasps at straws, or who fears the knife and will accept anything short of surgical attack, or knows of a relative or friend who had a new growth (usually benign) removed without recurrence, or the miracle seeker cannot be blamed for his support of cancer quacks.

It is the medical profession which, as guardian of the public's health, should report promptly to health authorities the active cancer quack as one practicing medicine without a license. If nothing is accomplished by this move, then organized medicine, as a county society, or as a state association should exert its pressure and political influence to see that legal and police power be used to padlock the quack's doors, or, wanting that, to have enacted such laws as will permit control of the charlatan.

Every physician should read "Cancer Charlatanism" and then, having knowledge of a quack, should carry out his duty to do everything in his power to put the quack out of business.

EDITOR.

1. Horton, C. E., Crawford, H. H., Maquire, C. P., Georgiade, N. G., and Pickrell, K. L.: Cancer Charlatanism, South. M. J. 49:567, 1956.
2. Washington News, J.A.M.A. 160:55 (advertising section), 1956.

25 YEARS AGO

Essential Hypertension*

"The clinical entity, essential hypertension, was described by Mahomed as early as 1879. In the studies of this brilliant clinician attention is called to the occurrence of certain symptoms. 'Persons who are subject to this condition suffer from many of the minor ailments which are characteristic of individuals who are the subject of chronic Bright's disease, such as malnutrition, cold hands and feet, shortness of breath and palpitation on exertion, imperfect digestion, bronchial and gastric catarrh, headaches (especially hemicranial), sometimes tinnitus and dimness of vision.' . . .

"Symptoms associated with the early stages of hypertension have not always been clearly differentiated from those due to complicating diseases such as arteriosclerosis with its involvement of cerebral, cardiac, and renal arteries. . . . However, numerous clinicians writing on various aspects of the problem have made frequent reference to symptoms seen in the early stages of hypertension at a time when complicating disease is unlikely. Treatment has often been directed against these symptoms and the value of medication in hypertension gauged by the relief obtained. . . .

"In the present communication, evidence is offered to show that the symptoms generally occurring in patients with uncomplicated essential hypertension are those of an associated psychoneurosis: (1) A psychoneurosis is shown to be present in these patients; (2) a comparison of their symptoms with those of a control group of neuropaths without hypertension, shows agreement in character, frequency, duration, course, and influence by suggestion and sedatives. . . .

"The distinction has been made between symptoms present in the early stages of hypertonia and those appearing later as a result of complicating vascular changes. The present study is concerned only with symptoms present before the onset of complicating disease. There is evidence that when hypertension has been present for a number of years it is associated with vascular changes. . . .

"The data for the present study were obtained as follows: (1) Records of 100 hypertensive outpatients covering visits in individual cases over a period of from one to seventeen years; (2) individual studies on 53 of these same patients coming under personal observation. Patients with evidence of renal, cardiac or cerebral disease were excluded. All patients showed a systolic blood pressure of 160 or higher, and the records indicated that this hypertension had been present for a period of from one to ten years. . . .

"*The Symptoms.* Table below gives the symptoms occuring in 100 cases. These represent a composite picture of complaints made over a period of years. They were usually of long duration, persisting for days, weeks, months or years, and were often severe in character.

The Frequency of Individual Symptoms In 100 Patients with Essential Hypertension.

Symptoms	Per cent Present
Headache	72
Pain	67
"Nervousness"	67
"Dizziness"	66
Fatigue and weakness	65
Insomnia	63
Constipation	57
Fatigue	55
Vasomotor symptoms	54
Weakness	38
Parasthesias	38
"Gas on Stomach"	37
Shortness of breath	34
Epigastric fullness	30
Anorexia	28
Heartburn	24
Nausea	21
Palpitation	18
Pain over cardiac area	15
Vomiting	14
Tremors	12
Choking sensation	12
Cough	9
Bad taste in the mouth	7
Fainting	6
Loss of weight	6

". . . (The) three general characteristics of these symptoms: (1) They are generally multiple and widespread, being distributed to almost every system and bodily part; (2) certain symptoms, such as pain, headache, constipation, and fatigue, are present in great frequency; (3) the duration of the symptoms is unusually long. Chart I tabulates this duration in 50 patients. It will be noted that 30 complained of symptoms over a period greater than ten years; 25 for fifteen or more years; 11 for thirty or more years. . . .

"In the present study the diagnosis of psychoneurosis was made when the following conditions were fulfilled: Symptoms characteristic of a psychoneurosis were present; physical examination revealed no organic disease which would satisfactorily account for these symptoms; the emotional history revealed that at the time faulty adaptations occurred, somatic symptoms developed. . . . Three general aspects were summarized; their multiplicity and widespread character; the high incidence of such symptoms as pain, headache and fatigue; the unusually long duration of the symptoms.

"The entire group of hypertensive patients with symptoms, personally observed, fulfilled the criteria mentioned for the diagnosis of a psychoneurosis. The symptoms were characteristic, the physical examinations negative, and the emotional histories revealed the presence of significant environmental difficulties closely related in time to the appearance or increase in severity of symptoms.

*Davis, David: The Nature of the Symptoms in Essential Hypertension, Am. J. M. Sc. 181:850, 1931.

"A Comparison of the Symptoms in Hypertension With Those of a Control Group of Patients With Psychoneurosis . . . compares the symptoms of 50 unselected hypertensive patients (average age fifty-one years) with those of 50 patients suffering with a neurosis (average age forty-eight years). . . . the symptoms compare not only closely in kind but remarkably so in their respective frequencies. This is rather striking and suggests that identical mechanisms are responsible for their production. Headache, dizziness, fatigue and other symptoms occur no more frequently in hypertension than they do in neurasthenia. . . .

"The Influence of Suggestion and Sedatives. Further evidence that the symptoms associated with hypertension are due to an accompanying psychoneurosis is offered by the known results of suggestion and sedatives. The influence of sedatives in hypertension, especially on the symptoms, needs no comment. It is general experience that they can be lessened with sedatives just as those of neurasthenia are allayed by the same means.

"The same is true of suggestion of any kind. The suggestion inherent in any form of "treatment" enthusiastically applied has been responsible for the large number of substances advocated.

"Conclusion. Evidence is offered to show that the symptoms generally occurring in patients with uncomplicated hypertension are those of an associated psychoneurosis: (1) A psychoneurosis is shown to be present in these patients. (2) A comparison of their symptoms with those of a control group of neuropaths without hypertension shows agreement in character, frequency, duration, course, and influence by suggestion and sedatives."

SOUTHERN MEDICAL NEWS

ALABAMA

Dr. Lee F. Turlington, councilor for Alabama of the Southern Medical Association, was elected to the national Board of Directors of the Planned Parenthood Federation of America. Dr. Turlington, a practicing gynecologist in Birmingham and past president of the Southern Obstetrical and Gynecological Society, has long been associated with the Planned Parenthood League of Alabama, and is now the chairman of its Board of Directors. He is associate professor of gynecology at the Medical College of the University of Alabama.

Dr. W. G. Thuss, Jr., attended the President's Conference on Occupation Safety in Washington, May 14-16, by invitation of President Eisenhower. Dr. Thuss, who is now completing a three-year fellowship in industrial medicine under Dr. Robert Kehoe of the Kettering Institute, University of Cincinnati School of Medicine, will return to private practice in the Thuss Clinic in Birmingham.

Dr. Alice McNeal, professor of anesthesiology at the Medical College of Alabama, has succeeded Dr. David A. Davis, as president of the Southern Society of Anesthesiologists.

ARKANSAS

Dr. William Luther Newton was honored with "Dr. Newton Day" in his home town of Smackover where he has served since opening offices in 1922.

Dr. Walter G. Selakovich, an orthopedic surgeon from New Orleans, has joined the Cooper Clinic in Fort Smith.

Dr. Max Roy, Forrest City, has been elected vice-president of the Mid-South Postgraduate Assembly of Memphis. Dr. Joe Verser, Harrisburg, is the retiring president.

Dr. Lewis M. K. Long has joined the staff in psychiatry at the University of Arkansas Medical School.

Dr. David M. Gould has succeeded Dr. I. Meschan as professor and head of the Department of Radiology at the University of Arkansas Medical Center. Dr. Gould had been affiliated with the Department of Radiology at Johns Hopkins Hospital since 1947.

Dr. W. G. Hensley, Charleston, was elected president of the Franklin County Medical Society. Dr. David L. Gibbons, Ozark, will serve as secretary-treasurer. Dr. C. C. Long, also of Ozark, is the delegate to the Arkansas Medical Society where he is vice-speaker of the House of Delegates.

Dr. M. L. Dalton, Brinkley, has been named president of the Monroe County Medical Society. The other officers are Dr. F. M. Wilson, Cotton Plant, vice-president, Dr. Terry Swaim, Cotton Plant, secretary, Dr. E. D. McKnight, Brinkley, delegate to the Arkansas Medical Society and Dr. J. P. Williams, alternate.

Dr. James M. Kolb has been elected president of the medical society of Clarksville. Dr. G. L. Hardgraves will serve as vice-president and Dr. G. R. Siegel will assume the duties of secretary-treasurer. The delegate and alternate delegate to the Arkansas Medical Society are Drs. W. R. Scarborough and R. H. Manley.

DISTRICT OF COLUMBIA

Dr. Bernard J. Michela has been appointed Medical Director of the Davis Memorial Goodwill Industries' new rehabilitation center. Dr. Michela is an instructor in the department of physical medicine at Georgetown University School of Medicine and a consultant in physical medicine and rehabilitation to the Bureau of Maternal and Child Welfare in

Continued on page 659

BOOKS RECEIVED

The Truth about Cancer. By Charles S. Cameron, M.D., Medical and Scientific Director, American Cancer Society. 268 pages, illustrated. Englewood Cliffs, New Jersey: Prentice-Hall, Inc., 1956.

Arteriosclerosis. A Symposium Presented by the Minnesota Heart Association and the University of Minnesota. Edited by Ancel Keys, Director, Laboratory Physiological Hygiene, University of Minnesota. 186 pages, illustrated. St. Paul, Minnesota: Minnesota Heart Association, 1955.

Therapy of Fungus Diseases. An International Symposium. Edited by Thomas H. Sternberg, M.D., Professor of Medicine (Dermatology) and Assistant Dean for Postgraduate Medical Education, and Victor D. Newcomer, M. D., Associate Professor of Medicine (Dermatology). 337 pages, illustrated. Boston, Massachusetts: The Little, Brown and Company, 1955. Price $7.50.

Anesthesia: Thief of Pain. By Sylvan M. Shane, D.D.S., Attending Anesthesiologist, Lutheran Hospital of Maryland. 87 pages, illustrated. New York: Vantage Press, Inc., 1956. Price $2.50.

A Handbook of Medical Hypnosis. Gordon Ambrose, L.M.S. S.A.; and George Newbold, M.B., B.S., M.R.C.S., M.M.S.A., D.R.C.O.G., D.C.H. 249 pages. Baltimore: The Williams & Wilkins Company, 1956. Price $5.00.

Modern Treatment Yearbook 1956. Edited by Sir Cecil Wakeley, Bt., K.B.E., C.B., LL.D., M.Ch., D.Sc., F.R.C.S., F.R.S.E., F.R.S.A., F.A.C.S., F.R.A.C.S. Fellow of King's College, London. 336 pages. Baltimore: The Williams & Wilkins Company, 1956. Price $6.00.

Basic Otolaryngology. By Francis L. Lederer, M.D., Professor and Head of Department of Otolaryngology, University of Illinois College of Medicine; and Abraham R. Hollender, M.D., Professor of Otolaryngology, Emeritus, University of Illinois, Chicago, and Clinical Professor of Otolaryngology, University of Miami School of Medicine. Fourth Edition. 424 pages, illustrated, 11 in color. Philadelphia: F. A. Davis Company, 1956. Price $6.75.

Strabismus, Diagnosis and Treatment. By Beulah Cushman, M.D., Associate Professor of Ophthalmology, Northwestern University Medical School, Chicago. 203 pages, illustrated. Philadelphia: Lea & Febiger, 1956. Price $6.00.

Gestation. Transactions of the Second Conference, March, 1955. Edited by Claude A. Villee, Ph.D., Assistant Professor of Biological Chemistry, Department of Biological Chemistry, Harvard Medical School. 251 pages. New York: Josiah Macy, Jr. Foundation, 1956. Price $5.00.

Noradrenaline. Chemistry, Physiology, Pharmacology and Clinical Aspects. By U. S. von Euler, M.D., F.A.C.P. (Hon.), Professor of Physiology, Faculty of Medicine, Darolinska Institutet, Stockholm, Sweden. American Lecture Series. 365 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $11.50.

Tropical Medicine for Nurses. By A. R. D. Adams and B. G. Maegraith, From the School of Tropical Medicine, Liverpool. Blackwell Scientific Publications. 305 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $7.50, approximately.

Textbook of Medical Physiology. By Arthur C. Guyton, M.D., Professor and Chairman of the Department of Physiology and Biophysics, University of Mississippi School of Medicine. 1030 pages, 577 figures. Philadelphia: W. B. Saunders Company, 1956. Price $13.50.

Gynecologic Cancer. By James A. Corscaden, M.D., Professor Emeritus of Clinical Gynecology, College of Physicians and Surgeons, Columbia University. Second edition. 537 pages. Baltimore: The Williams and Wilkins Company, 1956. Price $10.00.

Collagen Diseases. By John H. Talbott, M.D., Professor of Medicine, the University of Buffalo School of Medicine; and R. Moleres Ferrandis, M.D., Training Fellow in Arthritis of the Western New York Chapter of the Arthritis and Rheumatism Foundation. 225 pages. New York: Grune and Stratton, 1956. Price $6.50.

The Rochester Regional Hospital Council. By Leonard S. Rosenfeld, M.D., and Henry B. Makover, M.D. Published for the Commonwealth Fund by Harvard University Press, 1956. Price $3.50.

Tumors of the Skin. By Herbert Conway, M.D., Professor of Clinical Surgery, Cornell University Medical College. American Lecture Series. 252 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $13.50.

Culture and Mental Disorders. By Ralph Linton, Sterling Professor of Anthropology, Yale University. Edited by George Devereux, Director of Research, Devereux Foundation, Devon, Pennsylvania. 136 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $4.50.

Clinical Studies in Neurology. By Harry Lee Parker, M.D., Professor of Neurology, Mayo Foundation, Graduate School, University of Minnesota. 362 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $6.50.

Metabolism, Pharmacology and Therapeutic Uses of Gold Compounds. By Walter D. Block, Ph.D., Associate Professor of Biological Chemistry, Department of Dermatology, Medical School Research Associate, University of Michigan; and Kornelius Van Goor, M.D., Formerly Instructor, Department of Dermatology, University of Michigan Medical School. American Lecture Series. 65 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1956. Price $2.75.

Disturbances of Fluid Balance. Clinical Recognition and Management. By John H. Bland, M.D., Associate Professor of Medicine, University of Vermont College of Medicine. Second edition, 522 pages, 109 figures. Philadelphia: W. B. Saunders Company, 1956. Price $11.50.

Electrocardiography. Fundamentals and Clinical Application. By Louis Wolff, M.D., Assistant Clinical Professor of Medicine, Harvard Medical School. Second Edition. 342 pages, 199 figures. Philadelphia: W. B. Saunders Company, 1956. Price $7.00.

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Exclusive Publication: Articles offered for publication must be contributed solely to the Southern Medical Journal.

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1. Doe, J. E.: What You Should Know about It, New England J. Med. 243:435, 1950.

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BOOK REVIEWS

The Pathogenesis of Poliomyelitis

By Harold K. Faber, M.D., Professor Emeritus of Pediatrics and Director of Poliomyelitis Research, Department of Pediatrics, Stanford University School of Medicine. 157 pages. American Lecture Series. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $5.00.

This book is of value to those persons interested in virology, the historical aspects of poliomyelitis or the pathogenesis of this disease. It concerns the basic nature of poliomyelitis and deals at great length with controversial subjects such as the entrance of the virus into the body, the basic question of neurotropism, the fate of the virus after the initial invasion of body tissues, the primary site of virus multiplication, the role of the virus after its establishment in the central nervous system, the significance of viremia and the excretion of the virus into the alimentary tract. Lastly, the author deals considerably with prevention or alteration of poliomyelitis by immunization procedures.

This publication is excellent reference material although the author does not always present completely both sides of controversial issues.

Premature Infants

By Ethel C. Dunham, M.D., Formerly Associate Clinical Professor of Pediatrics, Yale University School of Medicine. Second Edition. 459 pages. New York: Paul B. Hoeber, Inc., 1955. Price $8.00.

This book is undoubtedly one of the most informative publications in pediatric literature. Dr. Dunham's vast experience has enabled her to cover the subject of prematurity in every detail and with such broad interpretation that the text is invaluable to physicians, nurses, dietitians, statisticians, students, obstetricians, social workers, public health groups, and to those interested primarily in research aspects of this disorder. Part I deals principally with diagnosis, incidence, etiology, and preventive measures, part II with the physiologic handicaps and related general care problems while part III is devoted to public health aspects such as death rates and the organized approach to the problem of prematurity.

The first edition of this book was published in 1948 and became well established as a medical classic. It is only natural that the second edition should be enthusiastically acceptable to the medical profession. This last edition has been brought up to date in every respect and unlike the first edition, has a hard cloth binding. References at the end of each chapter are very extensive and cover completely the available medical literature on prematurity. This publication should be easily available to all persons who deal even remotely with premature infants.

Obstetrical Anesthesia

By Bert B. Hershenson, M.D., Director of Anesthesia, Boston Lying-in Hospital, Clinical Associate in Anesthesia, Harvard Medical School. 375 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $9.50.

This book has been designed by Dr. Hershenson for the student of medicine, the practicing physician, and the obstetrician. The foreword is by Dr. Frederick C. Irving, who describes the book as scholarly, scientific and complete. Although the book was written for the teaching of obstetrical anesthesia, it is of equal value as a textbook for surgical anesthesia in general.

The historical background of anesthesia and also the individual anesthetic agents have been treated completely and interestingly. The discussion of reflex irritability and the factors which affect reflex irritability puts Reed's concept of a fear-tension pain syndrome in a true perspective.

Pain in labor is discussed from its anatomical and physiological aspects in a complete manner. He considers that control of pain in the obstetrical patient depends upon depression of the conscious mechanism of the perception and reaction to pain, interruption of the peripheral afferent pathways, or both.

In his discussion of premedication, the advantages of apomorphine-scopolomine medication during labor are clearly presented. The other analgesic and hypnotic drugs are also discussed in detail. In his discussion of the barbiturates he points out that they are primarily hypnotic and are not anesthetic agents. When used in heavy doses they may result in prolonged depression, delirium, or pulmonary complications as well as asphyxiation to the mother and baby. Complete discussion of the signs and stages of anesthesia are given as well as the management of emergency respiratory and cardiac derangements. Asphyxia neonatorum is considered in detail as to its cause, management, prevention and treatment.

The method of selection of the anesthetic agent, whether inhalation or regional, is discussed for each obstetrical condition. Special attention is given to the anesthetic management of complications in obstetrics such as heart disease, poliomyelitis, and diabetes.

In summary, this book is easy to read, well organized, and covers a subject which should be mastered thoroughly by the practitioner of obstetrics. The book is well indexed and serves as a reference volume as well as a textbook.

The Cornea

By Charles I. Thomas, M.D., Associate Clinical Professor of Ophthalmology, Western Reserve University School of Medicine; and Associate Ophthalmologist, University Hospitals of Cleveland, Ohio. 1,207 pages, illustrated. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $30.00.

The practitioner reading this review may at first question the need for a book of this length which restricts itself to such a small portion of the anatomy.

Continued on page 662

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SOUTHERN MEDICAL NEWS

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FLORIDA

Dr. Gimel Ortega has been certified by the American Board of Pediatrics.

Dr. George P. Daurelle has received certification as a Diplomate by the American Board of Radiology.

The Duval County Academy of General Practice elected the following officers for 1956: Dr. Joe E. Lanier, president; Dr. Jack Alford, vice-president; Dr. Charles Burke, secretary; Dr. Ben Franklin, treasurer; directors, Dr. Charles Henley, Dr. Elmer Leitner, and Dr. Sidney Halpern.

Dr. Curtis D. Benton, Jr., Fort Lauderdale, presented a scientific paper at the Fifth Congress of the Pan American Association of Ophthalmology in Santiago, Chile. Dr. Benton was also guest speaker at a meeting of the Uruguayan Ophthalmological Association in Montevideo, and attended a meeting of the eye section of the Amazonian Association in Manaos, Brazil.

Dr. John T. Goodgame, Clearwater, has been certified as a Diplomate of the American Board of Surgery.

Dr. Meredith F. Campbell, Miami, has been appointed editor for the United States for *Urologia Internationalis*, an international urologic journal published at Basle, Switzerland.

Dr. Joseph G. Seltzer, Orlando, has assumed the duties of president of the Congregation of Liberal Judaism at St. Petersburg.

Dr. Frank W. Putnam, professor and head of the department of biochemistry, College of Medicine, University of Florida, has recently completed a six weeks lecture tour of medical schools and scientific research institutes in Latin America. The tour was sponsored by the International Education Exchange Service of the U. S. State Department.

GEORGIA

Dr. Jack C. Norris, Atlanta, councilor to the Southern Medical Association from Georgia, along with fourteen other physicians from the United States, England, and Australia recently completed a three-day postgraduate course at the Memorial Center and Sloan Kettering Research Institute in New York. Subject matter included childhood tumors, tumors of the central nervous system, leukemia, bone and intrathoracic tumors, endocrine disorders in children and research problems in the conquest of cancer and leukemia.

Dr. Harriet E. Gillette, immediate past-chairman of the Section on Physical Medicine and Rehabilitation of the Southern Medical Association, has been awarded the Richard Kovacs Memorial Fellowship Fund. The fund was established to help defray the expenses of a qualified physician to attend the Second International Congress of Physical Medicine at Copenhagen, Denmark, August 20-24.

Dr. Irving Greenberg has been elected to the Executive Committee of the Atlanta Jewish Community Council.

Dr. Ernest W. Beasley, Jr., has been named a member of the Board of Directors of the Georgia Association for Retarded Children.

Dr. Robert E. Wells will serve as an instructor in surgery on a part-time basis at Emory University School of Medicine.

Dr. Sanford Matthews has been appointed associate Medical Director of Henrietta Egleston Hospital for Children.

Drs. Samuel Ambrose and Thomas Florence have been honored as recipients of the T. Leon Samuel Ambrose awards given by the Southeastern section of the American Urological Association.

Dr. E. Faxton Seay, Marshallville and Ft. Valley, has been named chief of the medical staff of the Peach County Hospital. Dr. Frank Vinson, Ft. Valley, is the new vice chief-of-staff, and Dr. Daniel E. Nathan, also of Ft. Valley, will serve as secretary.

Dr. Robert Monroe Lovvorn, Bowdon, recently celebrated his 90th birthday.

Drs. T. M. Martin, Jr., Bowdon, and T. E. Reeve, Carrollton, have been appointed chairmen of the Finance and Professional Education Committee of the Carroll County unit of the American Cancer Society.

Dr. McLaren Johnson, Atlanta, has been made an honorary member of the Professional Service Representatives Association.

Drs. Grady E. Longino, Samuel N. Dulin, Jr., and Folke Becker have joined the staff of the Dublin VA Hospital.

Dr. R. D. Walter, Calhoun, immediate past-president of the Northwest Georgia Council, Boy Scouts of America, has been elected the National Representative for the Northwest Georgia Council of the Boy Scouts of America.

Dr. William C. Retterbush, Valdosta, has been certified by the American Board of Surgery.

Dr. Samuel H. Hay, Toccoa, has been named a Diplomate of the American Board of Internal Medicine.

The officers for the Screven County Medical Society are Dr. Katrine Rawls Hawkins, Sylvania, president; Dr. James Freeman, vice-president; and Dr. G. B. Hogsette, secretary-treasurer.

Dr. S. L. Harp has been elected president of the Stephens County Medical Society. Dr. M. D. Pittard will serve as vice-president and Dr. C. L. Ayers as secretary.

Dr. Robert L. Patterson, Chickamauga, has been named president of the Walker-Catoosa-Dade Medical Society. Dr. Thomas E. Adkins, Rossville, is president-elect. The other officers are Dr. E. M. Townsend, Ringgold, secretary-treasurer and Drs. Fred H. Simonton, Chickamauga, and Louis A. Williams, Ringgold, delegates.

The Wayne County Medical Society has elected the following officers: Dr. Fred M. Harper, Jesup, president; Dr. R. A. Pumpelly, vice-president; Dr. Daniel H. G. Glover, secretary-treasurer; and Drs. J. W. Yeomans and Cecil Jacobs, delegates.

Dr. E. Carson Demmond, Savannah, has been named president of the Savannah Rotary Club.

Dr. Robert B. Gottschalk, Savannah, will serve as president of the Medical Arts Center, Inc. Dr. Jules Victor, Savannah, was elected vice-president.

Dr. Lawrence Lee, Jr., Savannah, has been appointed president of the Chatham-Savannah Tuberculosis and Health Association.

Dr. Brown Hill Boswell has become associated with the staff of the Moseley Hospital and Clinic in Donalsonville.

Drs. Charles D. Hollis, Jr., and Thomas D. Johnson, Albany, have been certified by the American Board of Internal Medicine.

Dr. Charles R. Smith, Columbus, has been named to membership on an advisory psychiatric committee for the Mental Hygiene Division of the State Health Department.

Dr. Grady E. Black, president of the medical staff of the Griffin-Spalding County Hospital, has been certified as a Diplomate of the American Board of Pediatrics.

The Griffin Exchange Club has named Dr. K. S. Hunt Griffin's "Man of the Year."

Dr. T. A. Sappinton, Thomaston, has filled the vacancy of county physician and clinician of Upson County created by the death of Dr. J. M. McKenzie.

A portrait of Dr. Daniel C. Elkin, formerly chairman of the department of surgery and Whitehead professor of surgery at Emory University School of Medicine, has been presented to the University.

Dr. Vernelle Fox, Atlanta, has succeeded Dr. George Bachmann as physician-in-charge of the state-owned Georgian Clinic for the treatment of alcoholics.

Dr. R. Frank Cary, Macon, will retire on July 1 from the office as health officer of the Macon-Bibb County Health Department. Dr. Cary has been health officer for 15 years.

Dr. E. M. Lancaster, Shady Dale, has recently been honored by the Order of the Eastern Star. Dr. Lancaster is grand sentinel of the grand chapter of the order.

Dr. Curtis F. Veal, Milledgeville, has joined the staff of Scott Hospital. He will continue to maintain his office in Ennis Heights.

Dr. J. E. Billings, Calhoun, will assume the duties of president of the Calhoun Rotary Club on July 1.

Dr. F. T. Fralick, Rome, formerly senior staff physician at Battey State Hospital in Rome, has become director of TB Control of the Fulton County Health Department. Dr. Paul S. Kemp has succeeded Dr. Fralick as senior staff physician.

Dr. Bradley B. Davis, Gainesville, has retired from active practice in pediatrics.

Dr. Guy O. Everhart, Loganville, has been appointed to the Board of Directors of the United American Life Insurance Company.

Dr. A. A. Rogers, Commerce, has been named chairman of the City Board of Health.

Dr. Edwin Leland Brackney joined the staff of the Medical College of Georgia as assistant professor of surgery on April 1.

Dr. W. M. Barton, Macon, has been elected president of the Georgia Society of Ophthalmology and Otolaryngology. Dr. Phinizy Calhoun, Jr., Atlanta, will serve as vice-president, and Dr. W. P. Rhyne, Albany, as secretary-treasurer.

KENTUCKY

Dr. Daniel C. Elkin, Lancaster, vice-president of the Kentucky Medical Foundation, has been appointed to membership on the University of Kentucky Board of Trustees. Dr. Elkin, president-elect of the American College of Surgeons, retired two years ago as professor of surgery at Emory University School of Medicine and moved to his farm in Garrard County.

Dr. Robert A. Orr, Mayfield, has been elected president of the Kentucky State Obstetrical and Gynecological society. Dr. Joseph Liebman, Frankfort, will serve as vice-president, and Dr. Edward Masters, Louisville, will assume the duties of secretary-treasurer.

Dr. William F. Lamb, whose resignation as deputy State health commissioner became effective in December, has returned to the State Health Department as director of local health services.

Dr. Leon Higdon, Paducah, member of the Kentucky State Medical Association Legislative Committee, testified on H. R. 7225 before the Senate Finance Committee.

Dr. John C. Bates, a 1952 graduate of the University of Louisville School of Medicine, has become associated with the Elizabethtown Clinic.

Dr. Alex J. Steigman, chairman of the department of pediatrics at the University of Louisville, has been named special consultant to the Communicable Disease Center of the Public Health Service, Department of Health, Education and Welfare.

Dr. Robert A. Hall has been elected president of the Johnson County Medical and Dental Society. Dr. Morris M. Hall will serve as vice-president and Dr. Augustus D. Slone as secretary-treasurer.

LOUISIANA

Under a contract with the International Cooperation Administration of the United States Department of State, the Tulane University School of Medicine has undertaken a project to supervise improvement of medical education in Colombia. Dr. Ernest Carroll Faust, the William Vincent professor of tropical diseases and hygiene and head of the division of parasitology at Tulane, will serve as field coordinator in Colombia for a minimum of two years. Tulane will be responsible for revising the curricula in the Colombian schools and for training young faculty members in the new program. Dr. Clifford G. Crulle, assistant dean of the Medical School and director of the division of graduate medicine, will be home coordinator for the project.

Portraits of three former chairmen of the department of pediatrics in the Tulane School of Medicine have been presented to the university. The three honorees, all Tulane graduates, were: Dr. William W. Butterworth, Baton Rouge; Dr. Lawrence R. DeBuys, New Orleans; and the late Dr. Robert A. Strong, Pass Christian, Mississippi.

Dr. James L. Elliott, clinical instructor of surgery at Louisiana State University School of Medicine, has been elected to membership in the American College of Chest Physicians.

Dr. Howard Mahorner, clinical professor of surgery at Louisiana State University School of Medicine, has been elected president of the Southeastern Surgical Congress.

Dr. Kennell P. Brown has received the distinguished service award as the outstanding citizen of the year in Jeanerette and vicinity.

Drs. Narcisse F. Thiberge and Peter B. Salatich, Sr., were honored by the medical staff of the Hotel Dieu Sisters' Hospital, New Orleans, for their 50 years of service.

The New Orleans Graduate Medical Assembly has elected the following officers for this year: Dr. Eugene H. Countiss, president; Dr. Charles L. Brown, president-elect; Dr. Edwin L. Zander, first vice-president; Dr. Barrett Kennedy, second vice-president; Dr. Joseph N. Ane, third vice-president; Dr. Maurice E. St. Martin, secretary; and Dr. Ralph M. Hartwell, treasurer.

MARYLAND

The Allegany-Garrett County Medical Society has elected the following officers: Dr. William Alfred VanOrmer, president; Dr. Benedict Skitarelic, vice-president; Dr. Leslie E. Daugherty, secretary; Dr. Leo H. Ley, Jr., treasurer; Drs. James T. Johnson, Jr., and Hilda Jane Walters, delegates; Drs. Frank T. Harrat and Dr. Leland B. Ransom, alternates.

Dr. Phillip Briscoe was re-elected president of the Anne Arundel County Medical Society. The other officers are: Dr. G. H. Faubert, vice-president; Dr. Howard Beard, secretary-treasurer; Dr. Randall McLaughlin, delegate; and Dr. Merton T. Waite, alternate delegate. Drs. Frank M. Shipley, Samuel Borssuck, and Albert L. Anderson will serve on the Board of Censors.

Dr. Robert A. Bier has been elected president of the Montgomery County Medical Society. Dr. Merrill M. Cross is the president-elect and Dr. Stephen N. Jones will serve as treasurer.

The Silver Spring Academy of Medicine has been re-activated. Dr. Peter Noble Lombard was elected president. Dr. Blaine Eig is the new vice-president and Dr. Charles Warfield is secretary.

Dr. Patrick B. Storey has accepted the position of acting chief of the Medical Service of Veterans Administration Hospital in Baltimore.

MISSISSIPPI

Dr. B. Z. Welch was honored recently by the Biloxi Lions Club on the completion of his 50 years of medical practice. Dr. Welch, who is 77 years of age, was cited for his remarkable career of civic, religious, and community activities in addition to a busy medical career. Dr. Welch has been a member of the Southern Medical Association continuously since 1909.

Dr. Elmer E. Pautler, chief of laboratory service in the U. S. Army Hospital at Fort Campbell, Kentucky, has been appointed associate professor of pathology at the University of Mississippi Medical Center.

MISSOURI

Dr. Carl F. Vohs, St. Louis, has been re-elected president of the St. Louis Blue Shield medical-surgical care plan. Drs. R. O. Muether and J. W. Thompson, both of St. Louis, will serve as first vice-president and secretary respectively.

The new officers of the medical staff of St. Luke's Hospital, Kansas City, are Dr. Richard H. Kiene, president; Dr. Druery Thorn, president-elect; Dr. Ernest L. Glasscock, vice-president; and Dr. John H. Gaskins, secretary.

Dr. R. R. Donley, Monett, is the new assistant physician for the Frisco Railroad.

The Federation of Child Health Centers honored the following Kansas City physicians for their services at thirteen child health centers: Drs. John Aull, Marvin Bordy, S. S. Cockerell, Milton Dodge, Mildred Duer, Charles P. Eldridge, G. E. Hughes, B. P. McDonald and James T. Van Biber.

Dr. George E. Kister, St. Charles, has been elected president of the Lincoln-St. Charles County Medical Society. The other officers are Dr. W. H. Poggemeier, St. Charles, secretary-treasurer; Dr. Louis P. Hetlage, Troy, and Dr. George E. Kister, delegates.

Dr. Bettye M. Caldwell, research associate in medical psychology and in pediatrics at the Washington

Continued on page 50

BOOK REVIEWS

Continued from page 655

If he merely scans the book he will quickly realize its value and alter his opinion.

The author brings together in one volume, material that can only be found by searching the domestic and foreign literature. The bibliography following each chapter indicates the scope of his research and also eliminates time-consuming labor for anyone desiring to delve deeper into related details.

The work has a practical presentation. The earlier chapters dealing with the basic concepts of anatomy, embryology and physiology of the cornea are not mere repetitions of facts but are written with a view toward relating these facts to an understanding of normal and abnormal appearances of a patient's cornea. The inflammatory, degeneration and neoplastic processes are dealt with in the same manner. A large section of the book describes corneal abnormalities seen with generalized diseases, and with contagious, dermatologic, metabolic and allergic diseases. The important considerations of corneal injury in its many forms are discussed from the diagnostic, therapeutic and prognostic standpoint. For the ophthalmic surgeon the final chapters are concerned with keratoplasty and other corneal surgical technics.

The many photographs of the cornea are of excellent quality and helpful in descriptions. The drawings, diagrams, charts and photomicrographs were selected wisely.

This is a textbook that will not be outdated too quickly.

Selection of Anesthesia

By John Adriani, M.D., Professor of Surgery, Tulane University of Louisiana School of Medicine, and

Director, Department of Anesthesiology, Charity Hospital. 327 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $6.50.

This book is more comprehensive than the title would indicate. The author has made the only logical approach to this important problem. Anesthesia should not be selected on a basis of "I believe or I do not believe in this or that type of anesthesia" but rather on a basis which this book provides: (1) pharmacology or clinical application of drugs in current use; (2) various diseases complicating the surgical condition after an understanding of these factors; and (3) the selection of the anesthesia.

This is an excellent book for residents both in anesthesia and other services and for the surgeon other physicians call upon to decide what type of anesthesia to be used in the absence of a qualified anesthesiologist.

The Pediatric Years

By Louis Spekter, M.D., Director, Bureau of Maternal and Child Hygiene, Connecticut State Department of Health. 709 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $12.50.

The author, widely experienced in the field of preventive medicine and public health, has written a useful book which contains certain information not available in other publications. This is a remarkably well-written guide for persons who work closely with the medical profession in problems of infant and child care. The book is divided into six sections. The first section deals with problems of pregnancy and early infancy and the second section with emotional and physical developmental problems. The third section is devoted to clinical entities and is so presented that the material is good for ancillary medical personnel but not complete enough for the physician. Section four, probably the most informative, is concerned with professional workers, their responsibilities and the available facilities for child care. This is a unique presentation in that there are very few sources of information that clarify the role of volunteer and official health services,—their names, services rendered, responsibility, and other descriptive material for the organizations listed. The fifth section is a condensation of standards that pertain to child care, health services, camps, housing, and specific disease situations. This, too, is useful as a guide for those concerned with the creation, maintenance or evaluation of such situations. The sixth section describes the technic of carrying out various pediatric procedures. In general the book is good as reference material.

Sexual Precocity

By Hugh Jolly, M.A., M.D., M.R.C.P., Consultant Paediatrician, Plymouth Clinical Area, London. 276 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $6.75.

Sexual precocity is usually considered a rare occurrence, so much so, that its presence often justifies isolated case reporting in the medical literature. Its rarity is responsible for the fact that there is little available information on the subject and the classification of this symptom complex is incomplete.

It is surprising that one person has been able to accumulate 69 patients with this disorder and, at the same time, have them accompanied by a wealth of such excellent clinical photographs. Approximately one-half of the book is devoted to a critical review of the subject of sexual precocity with discussions of important papers and of the author's own wide experience. The remainder of the book concerns individual case reports of the 69 patients. The monograph should be an important contribution to the fields of endocrinology and pediatrics and physicians interested in either of these specialties will find the book very informative.

Splenin A in Rheumatic Fever

By Alvin F. Coburn, M.D.; Lucile V. Moore, M.D.; Judith Wood, M.D.; and Mary Roberts, R.N., from the Rheumatic Fever Research Institute, Northwestern University Medical School, Chicago. 86 pages. Springfield, Illinois: Charles C. Thomas, Publisher. Price $3.75.

In 1935, Coburn and Pauli observed recurrence of activity in nine of twenty children with inactive rheumatic fever following splenectomy. It appeared that some substance other than streptococcal antigen or antibody was liberated when the spleen was manipulated and that this substance may have aggravated the rheumatic process. In 1945, Coburn consulted Ungar at the Nuffield Institute, Oxford, to determine whether Ungar's *splenin* might be a link in the rheumatic process. Ungar had been able to separate spleen extracts into two fractions, splenin A which decreased capillary permeability, and splenin B which increased bleeding time and capillary permeability. He also reported that the spleen and bone marrow played a part in hormonal regulation of the fibrinolytic system and the allergic reaction.

This book is an account of the preparation of splenin A and its trial for anti-inflammatory action over a period of three years in forty-seven children with acute rheumatic fever. The yield of splenin A, even when prepared by commercial laboratories, is extremely small and this fact makes it difficult to accumulate enough of the material for an extensive clinical trial. Brief clinical appraisals were presented for each of the patients treated. Control studies were not carried out but observations were made of concurrent comparable cases. The authors indicate that this is a limited study and they state frankly that splenin A did not modify the underlying rheumatic process or rheumatic susceptibility. It is their hope that this limited study will stimulate further investigations into the relationship of the spleen to inflammation and rheumatic fever.

Obviously much more work needs to be done before any clear ideas, pro or con, can be formed as to the physiologic or therapeutic effects of either splenin A or B. The book is concise and clear but the price, $3.75, seems much too high and one wonders why the relatively small amount of data was published in a book rather than in a journal where it would receive much wider circulation.

Saddle Block Anesthesia

By Ray T. Parmley, M.D., Director, Department of Anesthesiology, St. Francis Hospital. 59 pages. Ameri-

can Lecture Series. Springfield, Illinois: Charles C. Thomas, Publisher, 1955. Price $2.50.

The author has presented the facts about saddle block anesthesia and also spinal anesthesia in an unbiased fashion. This book should be read by both the proponents and opponents of this type of anesthesia. Questions of each group will be answered if read with an open mind. The technic used and indications and contraindications are concisely covered making the monograph valuable for learning the method and teaching it.

Feeling No Pain

By Bill O'Malley, cartoonist, caddy, laborer, newspaper artist, and insurance clerk. Author of Two Little Nuns, Golf Fore Fun, and Blessed Event. New York: Prentice-Hall, Inc., Publishers, 1955. Price $1.95.

This little book consists of humorous cartoons about doctors, nurses, and hospitals to while away the hours of convalescence. It will provide plenty of chuckles.

The Shoulder and Environs

By James E. Bateman, M.D., F.R.C.S., Orthopaedic Consultant, Sunnybrook Hospital, Toronto. 539 pages, illustrated. St. Louis: The C. V. Mosby Company, 1955. Price $16.25.

In this publication the author has provided not only a useful text, but an excellent reference that will be most valuable to orthopedic surgeons, general practitioners, medical students, and all concerned with management of shoulder dysfunction. For clinical purposes, in his discussion of the "shoulder," the author wisely refers to an entire region of the body including the neck, root of the neck, interscapular, scapular, clavicular, axillary, and pectoral zones. Also a very rational clinical classification is utilized in differential diagnosis and for purposes of discussion which makes analysis of the problems much less complex than would be the case using an anatomic or pathologic classification. Three predominant pain patterns are used in the classification: shoulder and neck pain, shoulder pain predominant, and shoulder plus radiating pain.

Evolutional and embryological development of the shoulder are covered in detail along with developmental anomalies of the region. In the section on physiology of the shoulder, all aspects of the origin and interpretation of pain in the shoulder region are very excellently discussed. The section on differential diagnosis is very complete and concise and is the real highlight of the publication; it is particularly recommended for the busy general practitioner who will not have time to read the book in its entirety. The subsequent chapters elaborate on the conditions in each of the three groups of the clinical classification with excellent descriptions of symptoms, physical findings, underlying pathology, etiology, and up-to-date conservative and operative types of treatment.

In addition there are chapters on nerve injuries and paralytic disorders, tumors of the shoulder region, and fractures and dislocations about the shoulder region. These are complete and well illustrated. The book is concluded by a section on management and evaluation of disabilities of the shoulder which is also superbly presented. The surgeon practicing orthopedics would certainly do well to familiarize himself with this portion of the book.

This publication is recommended as the most complete, best expressed source of information currently available regarding the shoulder region wherein every facet of development, diagnosis, pathology, etiology, and treatment of all pathologic conditions involving the region are adequately and capably presented.

Adaptive Human Fertility

By Paul S. Henshaw, Ph.D. 322 pages. The Blakiston Division McGraw-Hill Book Company, Inc., Publisher. Price $5.50.

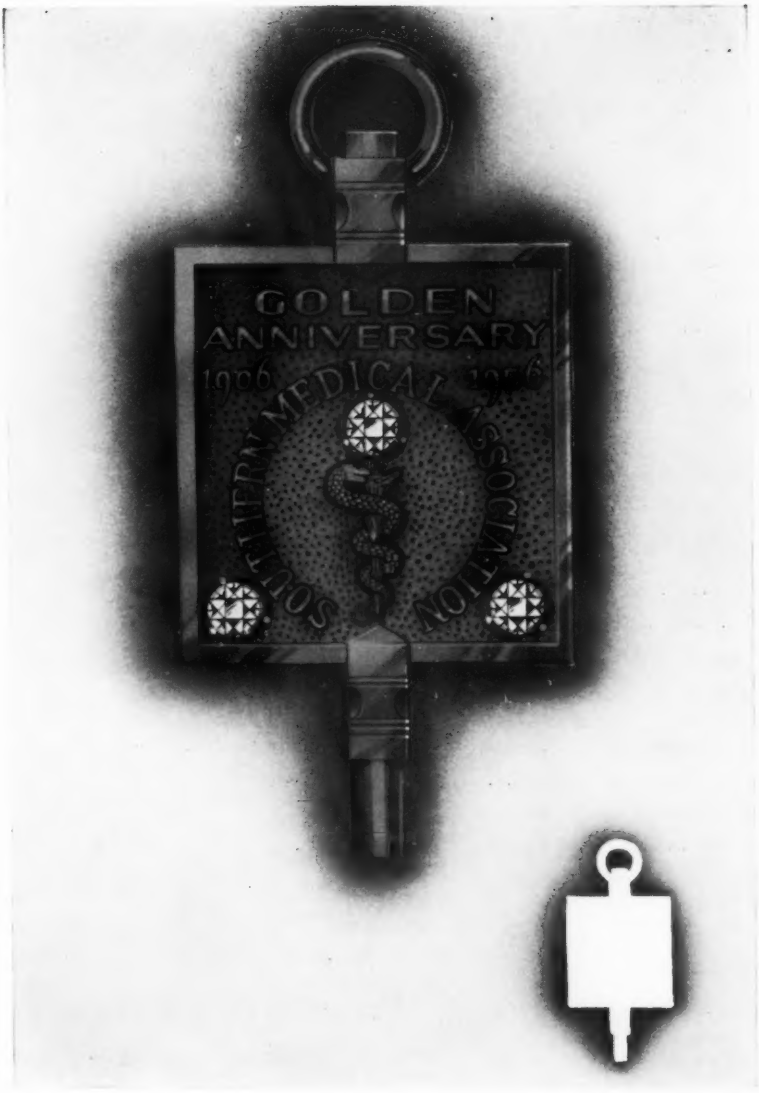
The author who is both a biologist and human ecologist has written an extremely thought-provoking book. Some of our best thinkers of today, Allan Gregg for one, have suggested that the very least some of us can do about the tremendous challenge presented by population problems is to think about it.

Although not written for popular consumption, the title of the book is perhaps unfortunate because the very people who need most to read it will be frightened away. It begins with a general discussion of the growth curve of population, growth mechanisms and some of the environmental elements affecting population growth. First, is a discussion of population in relation to renewable and non-renewable resources, food needs, the sustaining power of the earth and sea and the utilization of atomic and solar energies. The author concludes that serious difficulties are arising as a consequence of man's growth in numbers, that effective fertility guidance is essential if social degradation and spreading poverty are to be avoided, and that man's destiny will be determined by his ability to achieve a satisfactory relationship between his reproductive powers and his skill in developing and distributing the materials necessary for life.

The advantages, inherent conflicts and impediments of an intelligent plan for population control are discussed and then a considerable portion of the book is devoted to fertility management, beginning with primitive practices, proceeding to current practices and prospective practices.

In the final chapters population management practices are outlined and the author presents a plan of management which he terms teleogenic growth which represents planned populations on the basis of planned births as opposed to organic growth which represents unplanned population and unplanned births.

There is no question in this reviewer's mind that population growth and population problems are among the most serious dilemmas which face man today and none which are more complex. This book presents the problems in a concise and clear manner. This is not a book for the medical profession alone or for sociologists or for biologists, it is a book for the people. Unfortunately the people who need to be reached are not likely to see this book. One wonders if it should not be published in a less expensive pocket-sized edition, given an eye-catching title and cover and placed on the newsstands where it would receive the circulation it deserves.



(See opposite side for story and order form)

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Departure Date	..... hour ..... a.m. ..... p.m.

THE NAME OF EACH HOTEL GUEST MUST BE LISTED. Include the names of all persons for whom you are requesting reservations and who will occupy the room (s):

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.....	.....
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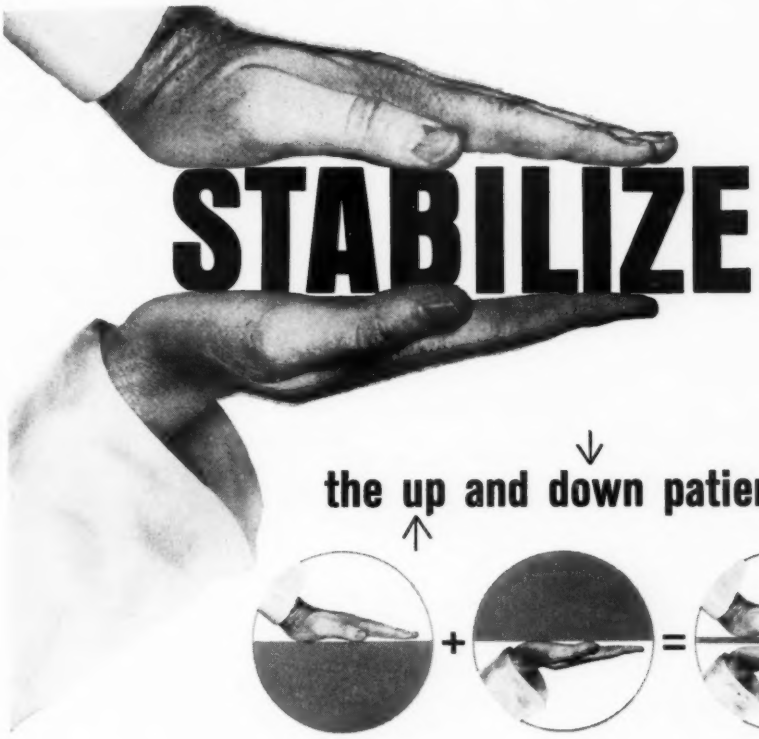

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1. Arnoff, B.: Personal communication. 2. Lazarte, J. A., and Petersen, M. C.: Personal communication.

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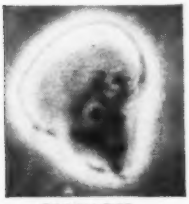

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References: 1. Davis, C. H.: J.A.M.A. 157:126 (Jan. 8) 1955. 2. Davis, C. H.: West. J. Surg. 63:53 (Feb.) 1955.

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Continued from page 662

University Medical School, has been appointed director of the new Washington University Child Evaluation Clinic. The clinic will primarily serve in the diagnosis and guidance of mentally retarded children.

Dr. Richard John Bing, professor of experimental medicine and clinical physiology and director of the Cardiac Clinic at the Medical College of Alabama, has been named chief of the Washington University Medical Services at Veterans Hospital and professor of medicine at the Washington University School of Medicine. His appointment will be effective July 1.

Dr. Frank B. Engley, Jr., professor and chairman of the Department of Microbiology, has been promoted to Acting Assistant Dean of the School of Medicine.

Dr. W. Ray Hepner, Jr., associate professor of Pediatrics, was appointed Medical Director of the State Crippled Children's Service.

Dr. Jerry William Brown will assume his new duties as assistant professor of anatomy at the University of Missouri School of Medicine on July 1. Dr. Brown is now with the department of anatomy, University of Pittsburgh School of Medicine.

Dr. Carl F. Vohs, St. Louis, has been installed as president of the Missouri State Medical Association. Dr. Walter S. Sewell, Springfield, was elected president-elect. Drs. Victor E. Scherman, St. Louis, R. E. Breuer, Newburg, and William J. Shaw, Fayette, will serve as vice-presidents. Drs. G. Ryse Bohrer, Jefferson City, and Jerome I. Simon, St. Louis, were re-elected secretary and treasurer respectively.

Dr. Charles H. Allen, Independence, has been presented the Veterans of Foreign Wars Community Service award for 1956.

Dr. Charles E. Martin, St. Louis, has been named treasurer of the American Academy of General Practice.

Dr. B. F. Byland, Maryville, has been appointed coroner of Nodaway County by the Governor to fill the unexpired term of the late Dr. L. E. Dean.

Dr. Emmett F. Hoctor, Farmington, was honored by Creighton University for his outstanding contributions to the University and the community.

Dr. Doyle C. Whiteman, Kansas City, has been elected president of the Kansas City Alumni Association of Pi Kappa Alpha fraternity.

The following officers have been elected to serve the medical staff of the Research Hospital, Kansas City: Dr. F. Stanley Morest, president; Dr. E. Kip Robinson, president-elect; Dr. Russell D. Shelden, secretary; and Dr. Ira T. Smith, treasurer.

Dr. Arthur R. McComas, Sturgeon, was awarded the Certificate of Merit of the University of Missouri Alumni Association. Dr. McComas has been a physician and surgeon for more than sixty-six years. The citation was made for his outstanding achievement and meritorious service in medicine during the many years of his practice.

Dr. Herbert Ensign Brown, an instructor of anatomy and physiology in the division of biology at Westminster College in Salt Lake City, will become assistant

Continued on page 56

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FOR YOUR PATIENTS WITH

Fat intolerance dyspepsia

Irritable bowel syndrome

Gallbladder dysfunction

OXSORBIL Capsules will permit the inclusion of suitable dairy and vegetable fats in the patient's diet.

POLYSORBATE 80 MAKES THE DIFFERENCE

This well balanced choleretic, cholagogic formula comes in two forms.

OXSORBIL® P.B. (contains phenobarbital and belladonna for patients also requiring spasmolysis and sedation)

OXSORBIL® *Plain*

IVC®

IVES-CAMERON COMPANY
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Bottles of 100 capsules
Literature on request

Introducing

A.P.C. WITH Demerol® Tablets

for more efficient
CONTROL OF *Pain*

Each tablet contains:		
Aspirin	**200 mg.**	**(3 grains)**
Phenacetin	**150 mg.**	**(2½ grains)**
Caffeine	**30 mg.**	**(½ grain)**
Demerol hydrochloride	**30 mg.**	**(½ grain)**

Adult dose: 1 or 2 tablets up to four times daily.

Bottles of 100 tablets. *Narcotic blank required.*

"Such a combination has proven clinically to be far more effective and no more toxic than equivalent doses of any of these used singly."*

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Demerol, brand of meperidine, trademark reg. U.S. Pat. Off.
*Bonica, J.J.; and Backup, P.H.: *Northwest Med.*, 54:22, Jan., 1953.

Ataractics and Holotherapy in

MENTAL and EMOTIONAL DISORDERS

Already clearly historical are the major successes due to use of the new ataractics, or tranquilizers, in mental and emotional disorders. Still vital, however, to enduring, optimal remission in *all* such disorders is the assurance of *adequate* nutrition — a therapeutic and prophylactic *fundamental*. For, the nervous system, even with the aid of the most efficacious drug, simply cannot function normally unless adequately supplied with essential nutrient factors.

Optimal treatment of all mental and emotional disorders whether mild or severe, acute or chronic, assures intake of optimally balanced, complete protein, vitamins and minerals — routinely, in adequate supply.

Patients with even the mildest of neuroses are under psychic stress. And stress increases the requirements for vitamins of the B complex. Deficiency of these vitamins or of essential amino acids instigates a tendency toward psychopathologic symptoms. A vicious cycle may thus be produced — to respond optimally only to total treatment, or *holotherapy*, which takes into account the *fundamental:* adequacy and balance of nutrients.

"Brewers' yeast is an excellent source of proteins of high biologic value and of the vitamins of the B complex.... When it is desired to give additional vitamins of the B complex and to add to the protein quota of the diet, this food can profitably be incorporated in other foods."*

VITA-FOOD Brewers' Yeast

an eminently valuable natural supplement — with these unique advantages:

- **Richest natural source of vitamin B complex factors plus nutritionally complete protein**
- **Optimal balance of amino acids and B complex factors**
- **Important source of minerals**

VITAMIN FOOD CO., INC. Newark 4, N. J.

*McLester, J. S., and Darby, W. J.: Nutrition and Diet in Health and Disease, ed. 6, Phila., Saunders, 1952, p. 195.

Continued from page 50

professor of anatomy at the University of Missouri on July 1. Dr. Grafton Adrian Smith has been appointed professor of surgery and Dr. Jason Neil Smith has been named instructor of medicine.

A memorial fund in honor of the late Dr. Frederick A. Jostes has been established at Washington University School of Medicine by his widow. The fund will be used to support the research program in the division of hematology. The late Dr. Jostes, who was a prominent St. Louis orthopedic surgeon, was an assistant professor of clinical orthopedic surgery at the time of his death in 1952.

Dr. John R. S. Shields, director of anesthesiology at the Children's Hospital, Winnipeg, Canada, and at the University of Manitoba, has been appointed assistant professor of anesthesiology in the department of surgery at Saint Louis University. Dr. Bela I. Hatfalvi was named instructor in anesthesiology.

Dr. Jules H. Kopp, St. Louis physician and surgeon and vice-president of the Missouri Social Hygiene Society, has been named an honorary life member of the American Social Hygiene Association.

NORTH CAROLINA

Dr. James M. Kelly, of Duke University Medical School's division of orthopedic surgery, has been selected as trainee of the National Institute of Arthritis and Metabolic Diseases. Dr. Kelly will be assigned

Continued on page 60

CITY VIEW SANITARIUM

For the diagnosis and treatment of nervous and mental disorders, and addictions to alcohol and drugs.

Established 1907

NASHVILLE, TENNESSEE

New... *and a Major Advance in Treatment of*

ASTHMA

MEDIHALER™

Fully effective nebulization with your favorite bronchodilator*

A plastic case; little larger than a package of cigarettes, contains Medihaler Oral Adapter and medication* (in shatterproof, spillproof vial).

Insert valve of medication vial snugly into Adapter.

Hold as shown, close lips around Adapter, and inhale while pressing vial down against Adapter.

Package is conveniently carried in pocket or purse. Inconspicuous, notably safe, dependable.

UNIFORM DOSAGE

SELF POWERED

ECONOMICAL

a) Unbreakable Adapter
b) No Medication Loss from Spillage or Oxidation

UNIFORM PARTICLE SIZE

80% between ½ and 4 microns radius

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***MEDIHALER-EPI™**

0.5% solution of epinephrine HCl U.S.P.

***MEDIHALER-ISO™**

0.25% solution of isoproterenol HCl U.S.P.

Simple to administer to children. Uniform dose, no spilling, no glass to break.

•

One or two applications abort most attacks. Rarely is more required.

follow this simple form of Rx

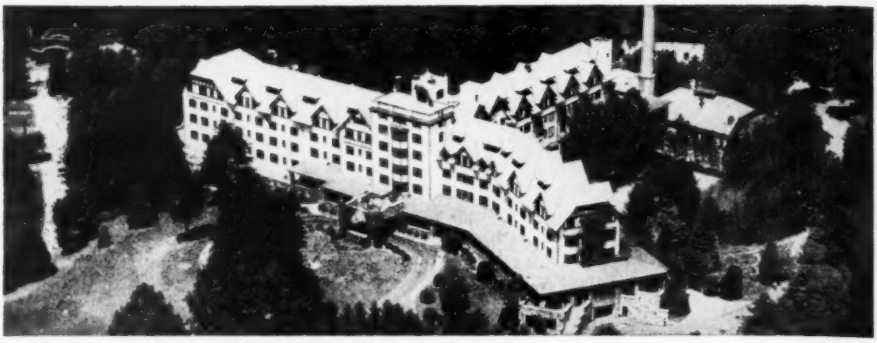
Riker
LOS ANGELES

Rx Medihaler-Iso and Medihaler Oral Adapter

ANOTHER RIKER FIRST

Appalachian Hall • Asheville, North Carolina

ESTABLISHED 1916



An Institution for the diagnosis and treatment of Psychiatric and Neurological illnesses, rest, convalescence, drug and alcohol habituation.

Insulin Coma, Insulin Sub-Shock, Electroshock and Psychotherapy are employed. The Institution is equipped with complete laboratory facilities including electroencephalography and X-ray.

Appalachian Hall is located in Asheville, North Carolina, a resort town, which justly claims an all around clime for health and comfort. There are ample facilities for classification of patients, rooms single or en suite.

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For rates and further information write APPALACHIAN HALL, ASHEVILLE, N. C.

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A PRIVATE PSYCHIATRIC HOSPITAL

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to help your patients past 40 correct . . .

biliary dyspepsia & constipation

Rehfuss[1] has stated that after 40, constipation is "the greatest single medical problem" and Shaftel[2] reports on the exceptional clinical results of Caroid® and Bile Salts in chronic constipation typical of this age bracket.

These cases do not respond to laxatives alone because associated complaints of flatulence and indigestion point to biliary dysfunction and digestive impairment as factors *coexisting* with constipation.

Caroid and Bile Salts Tablets are ideally suited for broad coverage in these cases. Through their 3-way action, they:

- INCREASE BILE FLOW
- IMPROVE DIGESTION
- PROVIDE GENTLE LAXATION

Tablets of Caroid and Bile Salts with Phenolphthalein have been clinically established and proved over the years. Try them in your next case of biliary dyspepsia and constipation.

Available—bottles of 20, 50, 100. For professional samples address:

American Ferment Company, Inc., 1450 Broadway, New York 18, N. Y.

CAROID AND BILE SALTS *tablets*

1. Rehfuss, M. E.: Indigestion, Philadelphia, W. B. Saunders Co., 1943, p. 322.
2. Shaftel, H. E.: J. Am. Geriatrics Soc. *1*:549 (Aug.) 1953.

fresh mixed

FOLBESYN*

VITAMINS LEDERLE

B+C

COMPLEX

assures full potency

Separate packaging of dry vitamins and diluent (mixed immediately before injection) assures the patient a more effective dose. May also be added to standard IV solutions.

Dosage: 2 cc. daily.

Each 2 cc. dose contains:

Thiamine HCl (B_1)	10 mg.
Riboflavin (B_2)	10 mg.
Niacinamide	50 mg.
Pyridoxine HCl (B_6)	5 mg.
Sodium Pantothenate	10 mg.
Ascorbic Acid (C)	300 mg.
Vitamin B_{12}	15 mcgm.
Folic Acid	3 mg.

Lederle

LEDERLE LABORATORIES DIVISION

AMERICAN Cyanamid COMPANY

PEARL RIVER, NEW YORK

*REG. U.S. PAT. OFF.

Continued from page 56

to the Duke clinic established for the study and treatment of arthritis.

Dr. John R. Overman, virus expert at the Rockefeller Institute for Medical Research, New York City, will join the Duke University Medical School faculty on July 1 as associate professor of bacteriology. The Medical School has been awarded the Lederle Medical Faculty Award for Dr. Overman.

Dr. Deryl Hart, Duke University surgeon, has been elected vice-president and president-elect of the Southern Society of Clinical Surgeons.

Dr. Paul F. Whitaker, clinical associate professor of medicine at the University of North Carolina School of Medicine, has been named president of the Medical Foundation of North Carolina. Other officers elected were: Dr. Adam T. Thorp, Rocky Mount, a vice-president; Dr. Shahane R. Taylor, Greensboro, secretary; and Dr. William M. Coppridge, Durham, treasurer.

Some of the world's most prized books and manuscripts in medical science were recently given to the Duke University Medical School. The gifts from the highly-valued Josiah C. Trent Collection in the History of Medicine were donated by Mrs. James H. Semans, whose late husband, Dr. Josiah C. Trent, assembled the collection. The total collection of more than 4,000 volumes and 2,000 manuscripts will eventually be turned over to the school.

Continued on page 66

Allen's

INVALID HOME

ESTABLISHED 1890

MILLEDGEVILLE, GEORGIA

For the treatment of

NERVOUS AND MENTAL DISEASES

Ground 600 Acres — Buildings, Brick

Fireproof — Comfortable — Convenient

Site High and Healthful

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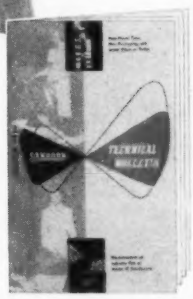
Terms Reasonable

"SANBORN" never leaves your office

A Viso-Cardiette owner finds that *service* — in many forms — is *always present.* It's just as if a Sanborn man were always standing by, ready to help him get the greatest usefulness from his Viso-Cardiette. Here are the ways Sanborn serves you:



Sanborn Branch Office men, centrally located throughout the country, have a *direct responsibility* towards your complete and continuing satisfaction with the Viso. They have special abilities, and complete stocks of supplies, accessories and instruments are quickly available.

Viso designers at the home office also may be consulted at any time on the technical aspects of special problems.

The popular, bi-monthly "Technical Bulletin" has been sent free-of-charge to owners for the past 35 years. It gives you and your technician helpful, current information on ECG and BMR testing techniques . . . typical questions and answers based on fellow-users' experience . . . facts about new Sanborn equipment and accessories.

A fourth way Sanborn serves you is through advanced instruction available as correspondence courses at small cost. The thousands who have completed these courses, together with those currently enrolled, attest to their value and acceptance.

Your local Sanborn Representative will be glad to tell you in detail about any of these regular services . . . that "never leave your office" when you're a Sanborn owner.

SANBORN COMPANY
Cambridge 39, Massachusetts

"... may be unique as a wide-spectrum antimicrobial agent that is bactericidal, relatively nontoxic, and does not invoke resistant mutants."[1]

Furadantin®

BRAND OF NITROFURANTOIN

in acute and chronic pyelonephritis, cystitis, prostatitis

Percentage of Effectiveness of Furadantin Against Various Strains of Bacteria in Vitro

	Aerobacter aerogenes	Proteus sp.	Paracolobactrum sp.	Micrococcus pyogenes	Streptococcus pyogenes	Escherichia coli	Pseudomonas aeruginosa
Furadantin	**82.1**	**66.6**	**31.2**	**91.9**	**93.9**	**60.0**	**13.3**
Antibiotic A	**71.4**	**55.5**	**25.0**	**93.5**	**96.9**	**66.0**	**26.6**
Dihydrostreptomycin	**14.2**	**25.9**	**12.5**	**38.7**	**27.2**	**28.0**	**6.6**
Antibiotic B	**3.5**	**0**	**0**	**66.1**	**63.6**	**0**	**2.2**
Penicillin	**3.5**	**0**	**0**	**27.4**	**39.3**	**0**	**0**
Antibiotic C	**14.2**	**7.4**	**18.7**	**46.7**	**72.6**	**22.0**	**11.1**

ADAPTED FROM PERRY[2]

Furadantin's "high degree of effectiveness against bacteria responsible for urinary tract infections is brought out by this study."[2]

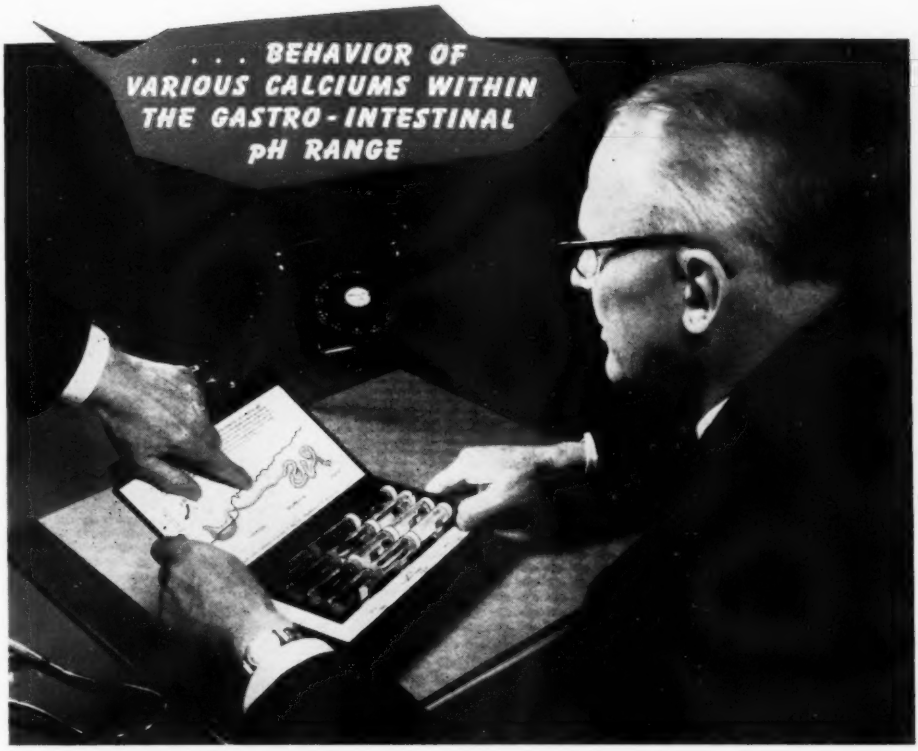
Furadantin dosage—simple and safe: Average adult dose is 100 mg., q.i.d., (at mealtime, and on retiring, with food or milk). Average daily dosage for children is 5 to 7 mg./Kg. in four divided doses.

SUPPLIED: Tablets, 50 and 100 mg., bottles of 25 and 100.
Oral Suspension, 5 mg. per cc., bottle of 118 cc.

REFERENCES: 1. Waisbren, B. A., and Crowley, W.: A.M.A. Arch. Int. M. 95:653, 1955. 2. Perry, R. E., Jr.: North Carolina M. J. 16:567, 1955.

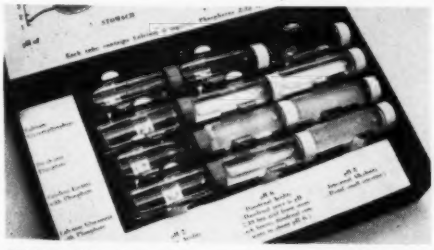
NITROFURANS—A NEW CLASS OF ANTIMICROBIALS—NEITHER ANTIBIOTICS NOR SULFAS

Eaton LABORATORIES



● Here's evidence* that shows why you prescribe bone health for your pregnant and lactating patients, Doctor, when you prescribe Cal-O-B Tablets. Ask the Warren-Teed man to show you this calcium and phosphorus solubility demonstration on his next visit.

● You'll see why the water-soluble, organic calcium glycerophosphate in Cal-O-B Tablets is the compound of choice . . . *supplying essential calcium and phosphorus that is soluble and absorbable throughout the gastro-intestinal pH range.*



CAL-O-B Tablets, Warren-Teed — each CAL-O-B Tablet contains calcium glycerophosphate 500 mg.; ferrous gluconate 200 mg.; vitamin D_2 (calciferol) 1,000 units; pyridoxine hydrochloride 1 mg.; ascorbic acid 50 mg. Trace minerals: manganese 0.12 mg.; iodine 0.14 mg.; fluorine 0.1 mg.; bromine 0.1 mg.; copper 0.75 mg.; potassium 5 mg.; zinc 1.0 mg.; magnesium 0.12 mg.; silicon 0.2 mg.; molybdenum 0.1 mg.; boron 0.1 mg.; cobalt 0.1 mg. Bottles of 100 tablets.

● Absorbed phosphorus is necessary for fixation of calcium in bone . . . and the m.d.r. of *both* doubles in your pre- and post-natal patients. When you prescribe Cal-O-B Tablets you need not leave the patient's phosphorus intake to dietary chance.

● That's why we urge you to prescribe bone health . . . soluble, assimilable calcium glycerophosphate . . . Cal-O-B Tablets, Warren-Teed.

*Evidence accumulated on calcium metabolism during a 3-year Warreen-Teed laboratory study and clinical investigation.

WARREN-TEED
Pharmaceuticals
THE WARREN-TEED PRODUCTS CO.
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A RESEARCH MILESTONE

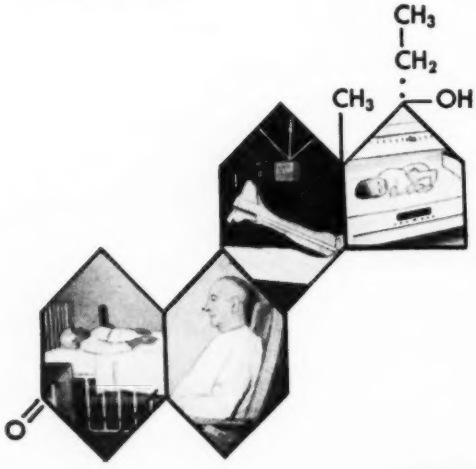
Nilevar*

(BRAND OF NORETHANDROLONE)

Searle's New and Practical Steroid Specifically for Protein Anabolism–

It has long been recognized that a substance which would promote protein anabolism would be of inestimable value in therapy. The androgens have this property, but unfortunately they also exert actions on secondary sex characteristics. These effects are commonly undesirable in therapeutic programs.

THE FIRST STEROID WITH ANABOLIC SPECIFICITY—Nilevar, the newest Searle Research development, therefore, meets a long desired clinical need because Nilevar presents the first steroid primarily anabolic for protein synthesis. Moreover, Nilevar is without prominent androgenic effects (only about one-sixteenth of that exerted by the androgens).



OBJECTIVE AND SUBJECTIVE RESPONSE—Orally effective, Nilevar therapy is characterized by retention of nitrogen, potassium, phosphorus and other electrolytes in ratios indicative of protein anabolism. Moreover, subjectively the patient observes an increase in appetite and sense of well-being.

WELL TOLERATED—Nilevar has an extremely low toxicity. Laboratory animals fail to show toxic effects after six months of continuous administration of high dosages. Nilevar should not be administered to patients with prostatic carcinoma. Nausea or edema may be encountered infrequently. Slight androgenicity may be evidenced on high dosage or in particularly responsive individuals.

MAJOR INDICATIONS—Preparation for and recovery from surgery; supportive treatment of serious illnesses (pneumonia, poliomyelitis, carcinomatosis, tuberculosis); recovery from severe trauma and burns; decubitus ulcers; care of premature infants.

DOSAGE—The daily *adult* dose is three to five Nilevar tablets (30 to 50 mg.) but up to 100 mg. may be administered. For *children* the average daily dose is 1 to 1.5 mg. per kilogram of body weight; individual dosages depend on need and response to therapy.

SUPPLY—Nilevar is available in uncoated, unscored tablets of 10 mg. G. D. Searle & Co., Research in the Service of Medicine.

*Trademark of G. D. Searle & Co.

SEARLE

For bigger appetites and better health—at any age

Redisol®

CRYSTALLINE VITAMIN B_{12}

MAJOR ADVANTAGES: Helps patients gain weight. Stimulates hemopoiesis. Elixir and Tablets readily blend with milk, juices and infant formulas.

Supplied as REDISOL Soluble *Tablets:* 25, 50, 100 *mcg.;* cherry-flavored *Elixir:* 5 *mcg.* per 5 cc.; *Injectable:* 30, 100, 1000 *mcg.* per cc.

SHARP & DOHME

Philadelphia 1, Pa.
DIVISION OF
MERCK & CO., INC.

AVOID RE-INFECTION FROM HIM IN VAGINAL TRICHOMONIASIS

KARNAKY reports in treating vaginal trichomoniasis ". . . approximately 39 to 47 percent of resistant cases are reinfections from the sexual partner."[1]

Symptom-free carriers. Most infected husbands of infected wives are asymptomatic. They are ". . . none the less a potential source of reinfection in wives successfully treated."[2]

Protect the wife. Karnaky recommends in recurrent cases of vaginal trichomoniasis that the husband wear a condom at coitus for as long as four to nine months. By the end of this time the trichomonads he harbors will usually die out.[3]

Prescribe high quality condoms. Take advantage of Schmid product improvements to win cooperation of the husband. According to the preferences and problems of your patient, prescribe Schmid condoms by name.

XXXX (FOUREX)® skins are made from the cecum of the lamb and are pre-moistened. They feel like the patient's own skin and *do not dull sensory effect.* RAMSES® natural gum rubber condoms are *different*—transparent, tissue-thin, yet strong.

Your prescription of Schmid condoms circumvents embarrassment, assures fine quality, provides essential protection.

Treat the wife. The Davis technique† with VAGISEC® liquid shows better than 90 per cent success in clinical data obtained by more than 150 physicians.[4] Unusual three-way attack with VAGISEC (originally "Carlendacide") actually *explodes* trichomonads. Liquid and jelly.

VAGISEC, XXXX (FOUREX) and RAMSES are registered trade-marks of Julius Schmid, Inc. †Pat. App. for

References: 1. Karnaky, K. J.: Urol. & Cutan. Rev. 42:812 (Nov.) 1938. 2. Lanceley, F., and McEntegart, M. G.: Lancet 1:668 (Apr. 4) 1953. 3. Karnaky, K. J.: J.A.M.A. 155:876 (June 26) 1954. 4. Davis, C. H.: West. J. Surg. 63:53 (Feb.) 1955.

JULIUS SCHMID, INC.
prophylactics division
423 West 55th Street, New York 19, N. Y.

The salicylated bile salts contained in CHOLOGESTIN have a double action. According to the 25th edition of the *United States Dispensatory*, published in 1955, ox bile extract increases both the salts and amount of bile, while salicylates have a hydrocholeretic effect and increase the volume.

CHOLOGESTIN contains both ox bile extract and sodium salicylate, plus pancreatin and sodium bicarbonate. Recommended dose as a choleretic or cholagogue, 1 tablespoonful in cold water after meals.

TABLOGESTIN, 3 tablets are equivalent to 1 tablespoonful of Chologestin.

FOR HEPATIC AND BILIARY DISORDERS

F. H. STRONG COMPANY
112 W. 42nd Street New York 36, N. Y. SMJ-6

Please send me free sample of TABLOGESTIN together with literature on CHOLOGESTIN.

DR.....

STREET.....

CITY.....ZONE.....STATE.....

Continued from page 60

SOUTH CAROLINA

Dr. H. R. Pratt-Thomas, Charleston, has been honored as the recipient of the American Cancer Society award for 1955.

Dr. John Van de Erve, Charleston, was elected vice-president of the Southeastern Dermatological Association.

Dr. Edwin Boyle, Jr., instructor in medicine at the Medical College of South Carolina, will be one of the principal speakers at a symposium on arteriosclerotic cardiovascular disease to be held in Basle, Switzerland, by the Swiss Academy of Science in August.

Dr. Roy B. McKnight, Charlotte, has been installed as president of the Tri-State Medical Association.

Dr. William H. Chapman, Whitney, celebrated his 75th birthday on March 3. Dr. Chapman, county

Continued on page 68

CLASSIFIED ADVERTISEMENTS

WANTED—General Practitioner or Internist—South Central Florida; retirement affords unusual opportunity to take over active, long established practice; lucrative income assured; fully equipped 6 room office; Florida license necessary; price and terms nominal to right party; state qualifications in query for details. Contact SMZ c/o SMJ.

RADIUM FOR SALE—Formerly used by Gynecologist. 85 mg. in seven platinum tubes. Contact DM c/o SMJ.

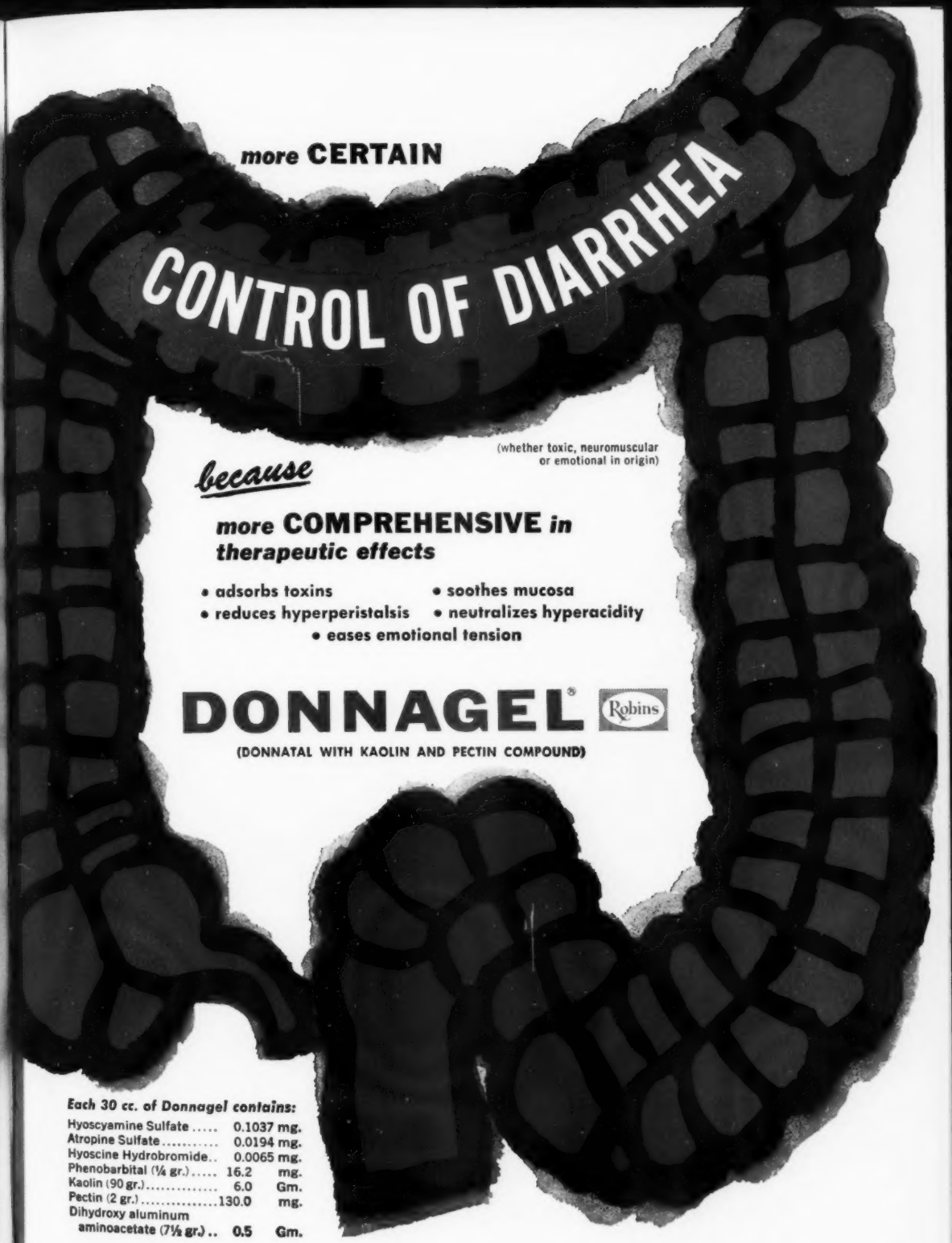
FOR SALE—Hugh Young urological table A-1 condition $750.00; Heidbring Gas Machine like new, $485.00; Picker Mobile X-ray Machine 30 M.A., A-1 condition, $975.00. A. H. SMULLIAN & COMPANY, P. O. Box 271, Station A, Atlanta 2, Georgia.

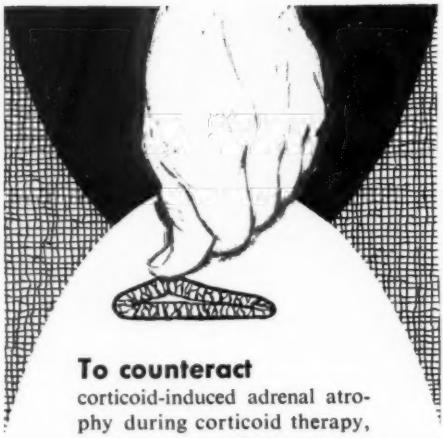
IMMEDIATE POSITIONS AVAILABLE for G. P. Residents at Lallie Kemp Charity Hospital, Independence, Louisiana. Stipend $500.00 per month. Requirements eligible for Louisiana Licensure, Graduate of Class A Medical School, approved internship. Write or Call C. C. Colvin, Lallie Kemp Charity Hospital, Independence, Louisiana.

FOR SALE—General Practice and Surgery, well established. Will introduce. Large clientele. Very reasonable. Reply to Box 6302, Station H, Atlanta, Georgia.

FOR SALE—Modern 8-room air conditioned EENT Clinic, completely furnished and equipped. Also three bedroom home. All on six beautiful lots. Warm dry climate in citrus section, Rio Grande Valley, Texas. Health demands immediate sale—cheap—will sell separately if desired. Contact Samuel T. Parker, M.D., 210 Canna Street, Pharr, Texas.

LOCATION WANTED—General Practitioner, 34 years, would like location in Texas or Oklahoma or would consider other state. Has Texas and Oklahoma license. Can furnish excellent references. Contact AE c/o SMJ.


more CERTAIN
CONTROL OF DIARRHEA
(whether toxic, neuromuscular or emotional in origin)
because
more COMPREHENSIVE in therapeutic effects
• adsorbs toxins
• soothes mucosa
• reduces hyperperistalsis
• neutralizes hyperacidity
• eases emotional tension
DONNAGEL®
Robins
(DONNATAL WITH KAOLIN AND PECTIN COMPOUND)
Each 30 cc. of Donnagel contains:
Hyoscyamine Sulfate ..... 0.1037 mg.
Atropine Sulfate ..... 0.0194 mg.
Hyoscine Hydrobromide.. 0.0065 mg.
Phenobarbital (¼ gr.)..... 16.2 mg.
Kaolin (90 gr.)..... 6.0 Gm.
Pectin (2 gr.)..... 130.0 mg.
Dihydroxy aluminum aminoacetate (7½ gr.).. 0.5 Gm.
Robins
A. H. ROBINS CO., INC., RICHMOND 20, VA.
Ethical Pharmaceuticals of Merit since 1878



To counteract
corticoid-induced adrenal atrophy during corticoid therapy, *routine support* of the *adrenals with ACTH is recommended.*

THIS IS THE PROTECTIVE DOSAGE RECOMMENDATION FOR COMBINED CORTICOID-ACTH THERAPY

- When using *prednisone* or *prednisolone:* for every 100 mg. given, inject approximately 100 to 120 units of HP* ACTHAR *Gel.*
- When using *hydrocortisone:* for every 200 to 300 mg. given, inject approximately 100 units of HP* ACTHAR *Gel.*
- When using *cortisone:* for every 400 mg. given, inject approximately 100 units of HP*ACTHAR *Gel.*

Discontinue administration of corticoids on the day of the HP*ACTHAR *Gel* injection.

HP*ACTHAR® *Gel*
(IN GELATIN)

The Armour Laboratories brand of purified adrenocorticotropic hormone—corticotropin (ACTH)

*Highly Purified

Unsurpassed in Safety and Efficacy
More than 42,000,000 doses of ACTH have been given

THE ARMOUR LABORATORIES
A DIVISION OF ARMOUR AND COMPANY
KANKAKEE, ILLINOIS

Continued from page 66

Doctor of the Year in 1950, has served the Whitney area for almost 50 years.

Dr. C. B. Harrell, Rock Hill, retired on March 1 after a 58-year career as a general practitioner. Dr. Harrell practiced in Colquitt County, Georgia, for 26 years before coming to Rock Hill in 1929.

Dr. Asa Paul Traywick, Cameron, was recently honored for his 50 years of service to the community. Representatives of the Young Men's Business Club presented Dr. Traywick with a silver tray and bronze plaque.

Dr. and Mrs. George Cullen Battle were presented a gift of silver in recognition of Dr. Battle's 22 years of service at the South Carolina Sanatorium. Dr. Battle retired as a member of the medical staff on January 1.

Dr. R. P. Walton, of the department of pharmacology at the Medical College of South Carolina, has been named to the Abel Award Committee of the American Society for Pharmacology and Experimental Therapeutics.

Dr. Dale Groom, department of medicine at the Medical College of South Carolina, has been elected a Fellow of the American College of Physicians.

Dr. George W. Smith, Columbia, has been elected president of the South Carolina Radiological Society. The other officers are Dr. Willis S. Hood, Greenville, vice-president, and Dr. Samuel W. Lippincott, Charleston, secretary-treasurer.

Continued on page 70

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Continued from page 68

The South Carolina Academy of General Practice has elected the following officers for 1956: Dr. Harvey W. Mead, Pendleton, president; Dr. Charles N. Wyatt, Greenville, president-elect; Dr. Gustave P. Richards, Charleston, vice-president; Dr. G. W. Price, Spartanburg, director; Dr. William T. Hendrix, Spartanburg, chairman of the board of directors; and re-elected Dr. Horace M. Whitworth, Greenville, secretary-treasurer.

TENNESSEE

Dr. Harold D. West, president of Meharry Medical College, received on behalf of the college, an AMA award of special merit for television pioneering. "Medical Horizons," a television series sponsored by Ciba Pharmaceutical Company, was telecast from the College on February 27. The program dramatized research work now in progress at Meharry with radioactive gold in the treatment of cancer.

Dr. J. Wesley McKinney, Memphis, has been named executive secretary for North of Panama, for the Pan American Association of Ophthalmology.

Dr. K. M. Kressenberg, Pulaski, has been re-elected president of the Giles County Medical Society. Dr. D. M. Spotwood will serve as vice-president and Dr. Harvill Hite as secretary.

Dr. F. Tremaine Billings, Nashville, has been nominated to membership on the Princeton University Board of Trust.

The American Cancer Society has honored Dr. Charles C. King, Memphis, with an award for outstanding service. The presentation was made by Dr. Ralph R. Braund, Memphis, president of the Tennessee Division of the American Cancer Society.

Dr. Robert M. Finks, Nashville, has been appointed chief-of-staff of the Baptist Hospital in Nashville. The other chiefs of services are: Dr. Harry Moore, anesthesiology; Dr. Leslie Rowe Driver, eye, ear, nose and throat; Dr. J. A. Kirtley, Jr., general surgery; Dr. R. K. Galloway, general practice; Dr. J. Lanier Wyatt, internal medicine; Dr. Scott Bayer, obstetrics-gynecology; Dr. George K. Carpenter, orthopedics; Dr. Frank Womack, pathology; Dr. E. E. Wilkinson, pediatrics; Dr. J. M. Ivie, roentgenology; and Dr. C. E. Haines, urology.

Dr. Avery T. King, Oak Ridge, has assumed the duties of urologist at the Oak Ridge Hospital.

Dr. L. W. Nabers, Morristown, has been installed as president of the Mid-South Postgraduate Medical Assembly. Dr. William G. Stephenson, Chattanooga, was elected vice-president.

Dr. Oscar N. Torian, Sewanee, has been honored as "Outstanding Citizen of 1955 in Franklin County."

Dr. Carolyn Beard, Maryville, has succeeded Dr. W. N. Dawson, as director of the Blount County Health Department.

Dr. Dan Thomas, Knoxville, has been elected president of the Knoxville Welsh Society.

Continued on page 72

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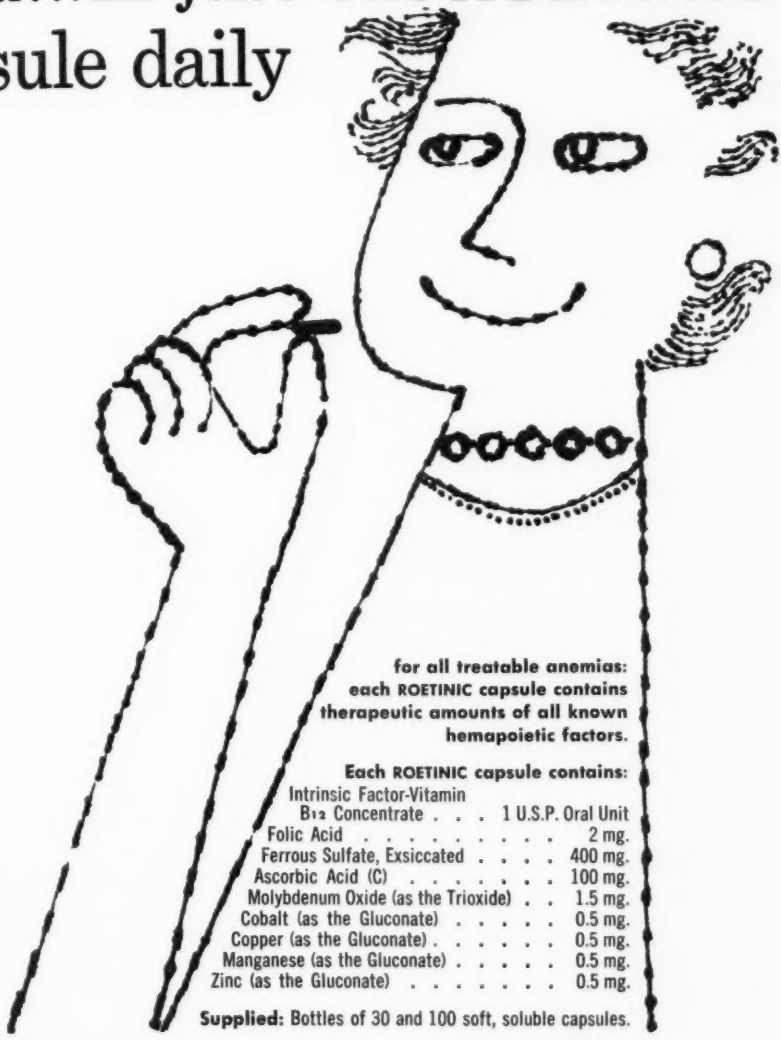

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Continued from page 70

Dr. Park Niceley, Knoxville, has been named to the International College of Surgeons.

Dr. DeWitt Owen, Franklin, has purchased the Schell Hospital in Franklin.

Dr. Gerald Johnson, Winchester, has been elected the first president of the Franklin County Chapter of the American Cancer Society.

Dr. R. L. Maloney, McMinnville, is the recipient of the VFW Citizenship Award for 1956.

Dr. Emil Meirowsky, professor emeritus in dermatology, School of Medicine, University of Cologne, Germany, has been honored on his eightieth birthday by the Society of Investigative Dermatology, for his past and continued contributions in dermatologic research especially in the field of melanin in the skin. Dr. Meirowsky, an honorary member of the Society, now lives with his son, Dr. Arnold Meirowsky in Nashville.

Dr. T. S. Hill, superintendent of Gailor Psychiatric Hospital and head of the department of neurology and psychiatry at the University of Tennessee College of Medicine, has been granted a year's leave of absence to become director of the clinic for the study and treatment of alcoholics.

TEXAS

Dr. Robert Hausman, Atlanta, Georgia, will assume the duties of medical examiner for Bexar County, Texas, on July 1.

Dr. J. G. Sewell, Belton, has been installed as president of the Belton Chamber of Commerce.

Dr. Titus H. Harris, Galveston, has been honored as the recipient of the Hogg Foundation Award in recognition of his outstanding contributions in the field of mental health.

The American Academy of Obstetrics and Gynecology has inducted the following Texas physicians: Dr. William J. Hegedus, Amarillo; Dr. Ben K. Howard, Dallas; Dr. J. L. Jackson III, Wichita Falls; Dr. Garland H. Lang, Midland; and Dr. Walter E. McRee, Jr., Port Arthur.

VIRGINIA

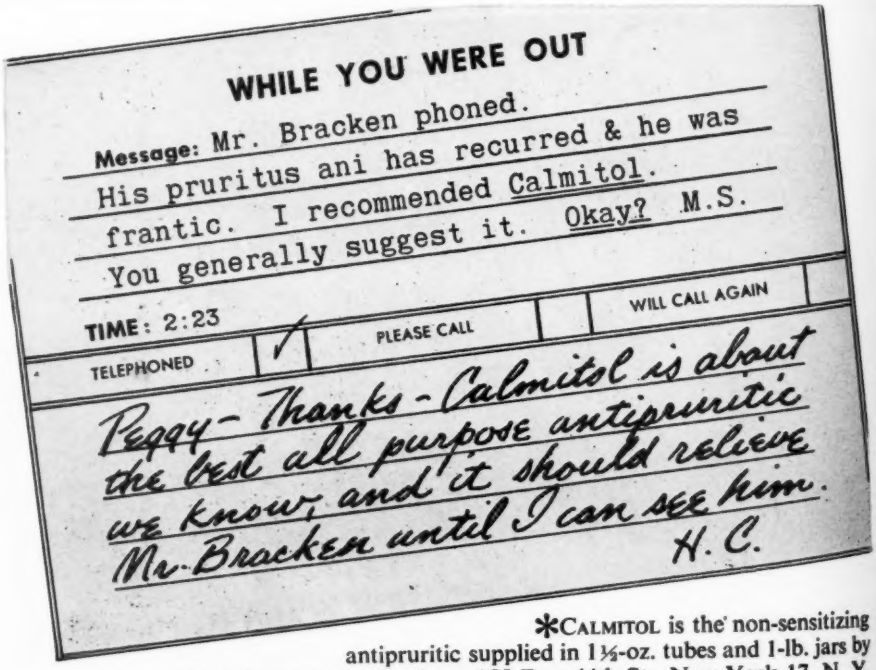
Dr. M. M. Bray, Suffolk, has been elected president of the Tri-County Medical Society. Dr. H. L. Gardner, Franklin, will serve as vice-president and Dr. J. E. Rawls, Jr., Suffolk, as treasurer.

Dr. W. Norman Thornton, Charlottesville, was elected assistant secretary-treasurer of the South Atlantic Association of Obstetricians and Gynecologists.

Dr. Ed Bryce has been named president of the Richmond Eye, Ear, Nose and Throat Society. Dr. C. N. Romaine has assumed the duties of secretary-treasurer.

Dr. Frank E. Tappan, Berryville, has been installed as president of the Virginia Academy of General Practice. The officers elected to serve with Dr. Tap-

Continued on page 77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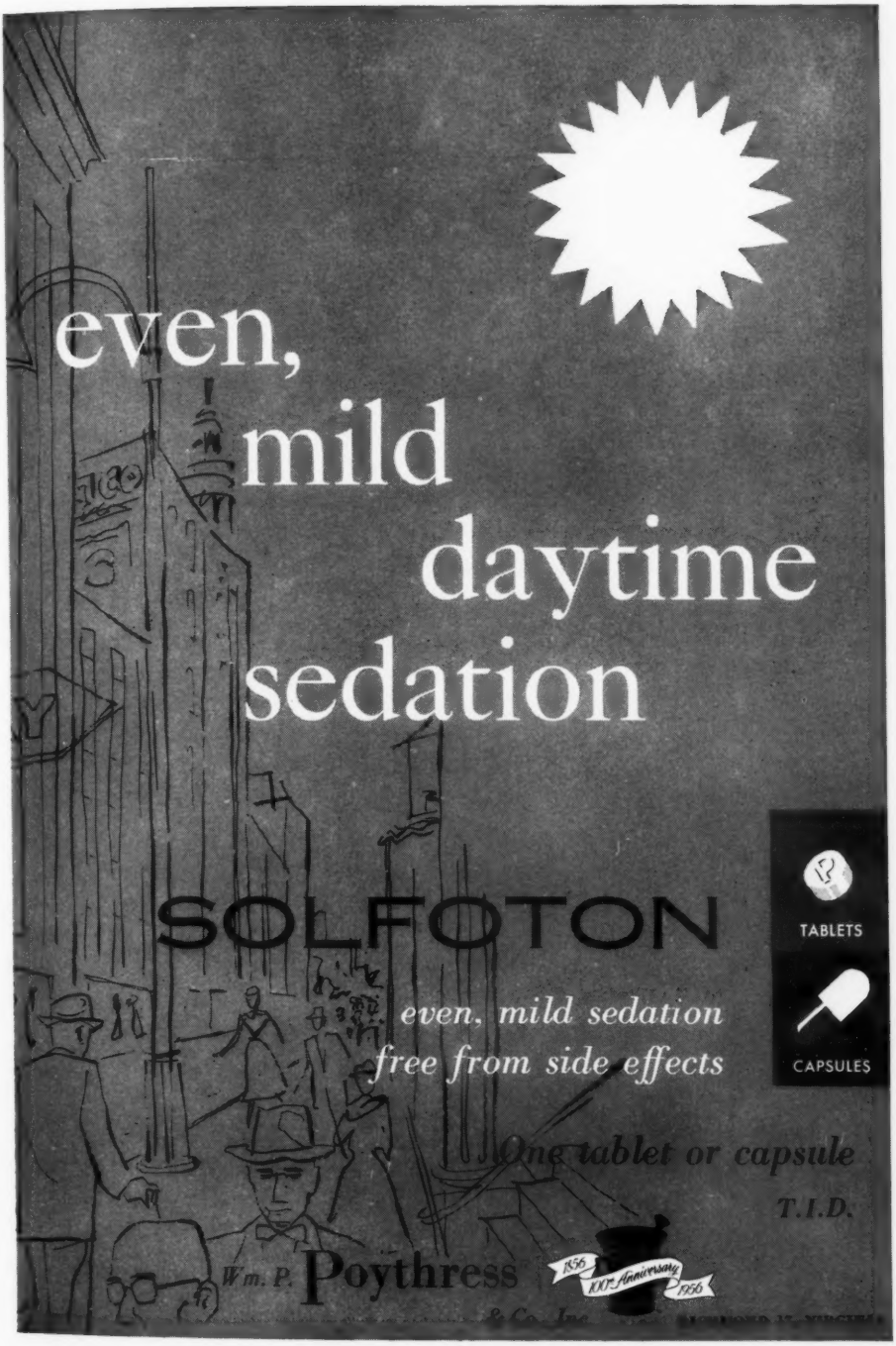
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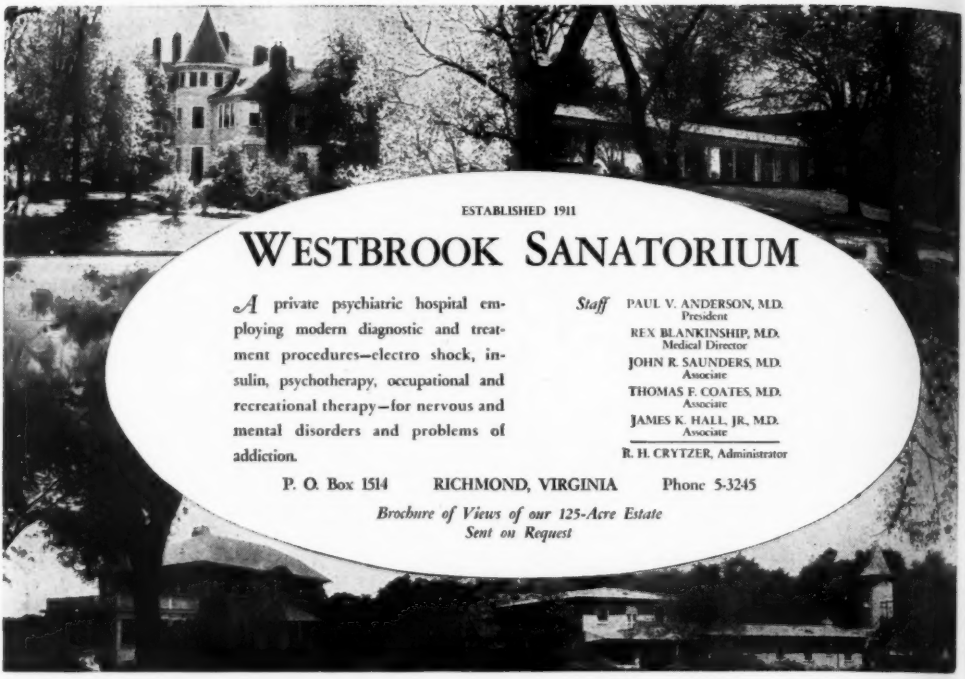
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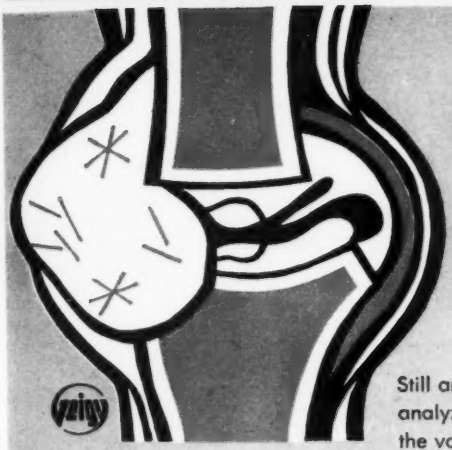

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1. Denko, C. W.; Ruml, D., and Bergenstal, D. M.: Am. Pract. & Digest Treat. 6:1865, 1955.
2. Holbrook, W. P.: M. Clin. North America 39:405, 1955.

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Continued from page 72

pan are: Dr. Malcolm H. Harris, West Point, president-elect; Dr. Frank A. Farmer, Roanoke, vice-president; Dr. R. G. McAllister, Richmond, secretary; and Dr. William A. Young, Richmond, treasurer. Drs. R. Bruce Lawrence, Richmond, John L. Harris, Jr., Roanoke, Walter C. Caudill, Pearisburg, and Thomas L. Lucas, Alexandria are newly elected members of the Board of Directors.

Dr. W. Geoffrey Wysor, Halifax, has been appointed to the staff of the department of medicine of the University of North Carolina in Chapel Hill. Dr. Wysor will continue his local practice.

Dr. William T. Sanger, president of the Medical College of Virginia, has announced the following promotions from assistant to associate professor: Dr. Christian V. Cimmino in clinical radiology; Dr. Charles W. Massey in radiology; and Dr. Joseph C. Parker in clinical obstetrics.

Dr. W. T. Thompson, Jr., Richmond, has been re-elected president of the Virginia Association for Mental Health.

Dr. Robert W. Woodhouse has been honored as First Citizen of 1955 at Virginia Beach. Dr. Woodhouse has practiced medicine in Princess Anne County and Virginia Beach since 1913.

Dr. William S. Sloan, Petersburg, participated in the Fort Lee review in observance of National Defense Week. As the area's senior active Reserve Officer, with the rank of Colonel, Dr. Sloan represented the thousands of Reservists all over the country.

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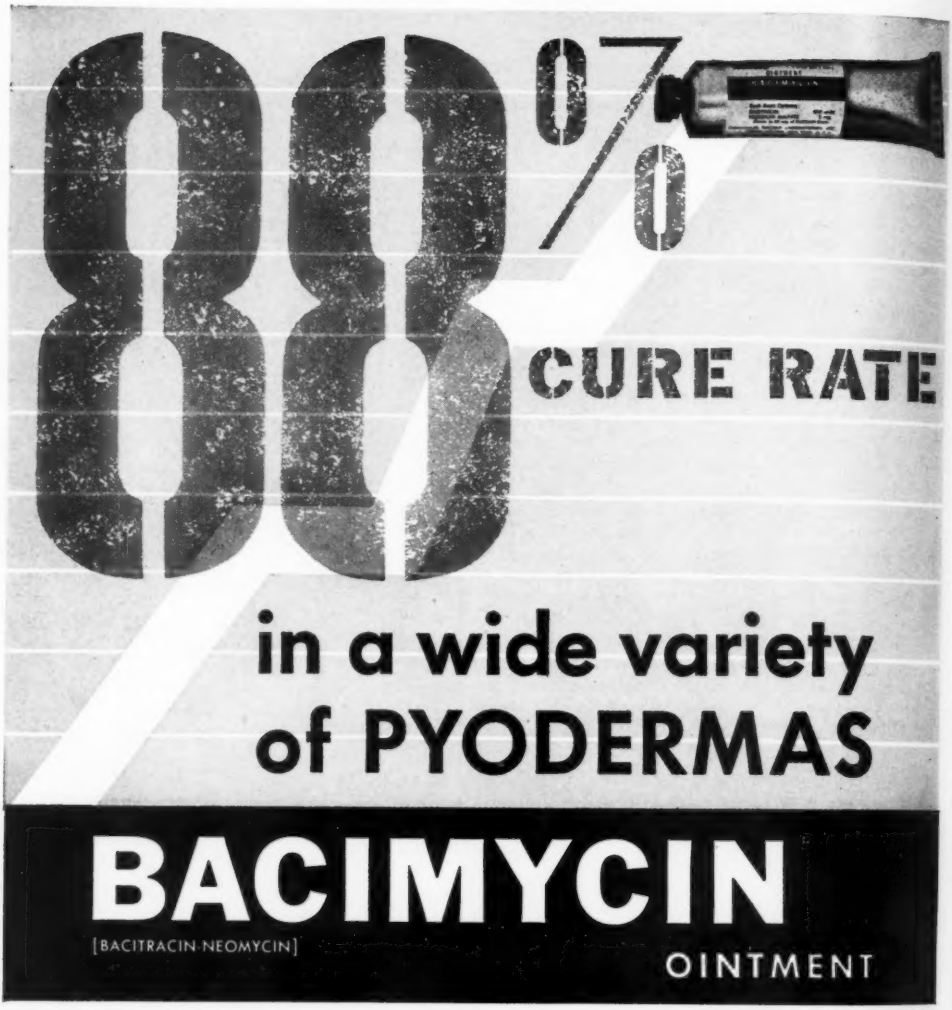

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1. Greenhouse, J. M., and Ryle, W. C.: A.M.A. Arch. Dermat. & Syph. 69:366, Mar., 1954.

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